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ACUTE GENERALIZED MILIARY TUBERCULOSIS IN ADULTS*

A Clinicopathological Study Based on Sixty-Three Cases Diagnosed at Autopsy

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ACUTE generalized miliary tuberculosis is a condition that results from the sudden and often overwhelming hematogenous dissemination of tubercle bacilli from an established focus to many of the organs of the body. The large number of small, acute tubercles that develop in these organs have been said to resemble millet seeds in size and appearance, whence stems the adjective "miliary." The clinical course is so varied that diagnosis before death is often not achieved. The condition should be rigidly differentiated from the various forms of nonprogressive or slowly progressive, more or less localized forms of disseminated tuberculosis. The hematogenous dissemination of occasional tubercle bacilli from chronic foci in the lungs or elsewhere frequently results in the various forms of chronic disseminated tuberculosis so often seen at autopsy. Pennington[1] found that 68 per cent of 200 cases of pulmonary tuberculosis at autopsy showed extrapulmonary foci of a chronic type, lesions that Krause[2] terms "benign generalizations" of pulmonary forms of tuberculosis. Hegler[3] points out that when occasional tubercle bacilli are released, producing isolated tubercles in one or two additional sites, the disease has in a sense become generalized but is still quite distinct from acute generalized miliary tuberculosis. Kayne, Pagel and O'Shaughnessey[4] believe that acute, fatal disseminations occur in an extremely small percentage of affected persons but that some 40 per cent show evidence of hematogenous dissemination at autopsy. Most of the cases fall in the group that these authors term "abortive hematogenous dissemination," and the extrapulmonary lesions are generally nonprogressive.

One must recognize, therefore, that disseminated tuberculous infection may appear in several forms. One extreme is the acute, progressive disease, which is the subject of this survey; the other extreme is the chronic, nonprogressive extrapulmonary tuberculous lesion, which seldom, if ever, causes death.

All the autopsy reports for the Boston City Hospital over a five-year period (1937-1941, inclusive) were reviewed. In selecting cases for the series, two important exceptions were made, as follows: none of the autopsy material from the Sanatorium Division was utilized, and cases in patients less than twelve years of age were excluded owing to the fact that the autopsy material included a disproportionately small number of children. We have thus concerned ourselves exclusively with the condition as it occurred in adults in this, a general, hospital.

INCIDENCE

General

Acute generalized miliary tuberculosis is generally considered to be a rare condition. Lewison et al.[5] reported that 1.09 per cent of 8800 consecutive autopsies at Cook County Hospital showed the condition. Our own data indicate that 1.55 per cent of the 4066 cases autopsied at the Boston City Hospital between 1937 and 1941 showed acute generalized miliary tuberculosis. Of considerably greater interest is the frequency with which the condition is present in cases showing some more chronic type of tuberculosis. Fishberg[6] states that of patients suffering from pulmonary tuberculosis in any of its forms, about 1 in 20 dies with symptoms of miliary dissemination of tubercle bacilli, and approximately the same figure is given by Simmonds.[7] In Lewison's series the condition was found in 11.9 per cent of tuberculous cases. Auerbach[8] reviewed 1656 consecutive autopsies on patients with tuberculosis, in 17.9 per cent of which acute generalized miliary tuberculosis was demonstrated. We reviewed autopsies on 4066 patients, in 310 of which (7.6 per cent) tuberculosis of some sort was present. In this group of 310 cases, there were 63 cases of acute generalized miliary tuberculosis (20 per cent). Our figures are somewhat analogous to Lewison's in that they represent the incidence of the condition at

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autopsy in a general hospital, but they are not truly analogous in that owing to the nature of the autopsy material children have been excluded from the series.

By Sex

Litten,[9] in one of the classic articles on the subject, stated that acute generalized miliary tuberculosis is more frequent in men that in women, and Fishberg[6] is in agreement. Hartwich,[10] however, reviewing 200 cases of the disease, found that 51 per cent of the patients were females and 49 per cent were males. In our series of 63 cases, there were 44 men (70 per cent) and 19 women (30 per cent). Of the 310 patients in whom some type of tuberculosis was found at autopsy, however, 69 per cent were males and 31 per cent were females. Hence the sex incidence of acute generalized miliary tuberculosis in this series is not significantly different from that for tuberculosis of all types. Furthermore, in this hospital more autopsies are permitted on men than on women, and we are of the opinion that the alleged sex difference in the incidence of the condition is more apparent than real.

By Age

That the disease may occur at any age is generally agreed. Its occurrence in the earliest weeks of life has been noted by Hegler,[3] who reviewed the cases of this type reported up to 1923. Transmission of the infection to the unborn child by the maternal and placental circulations has been suggested, and we noted 1 case in which such a process may have occurred.

The highest incidence of the disease is said by some authors[3, 8, 11] to occur in the second and third decades. In Hartwich's[10] series the peak incidence occurred in the first decade. Amberson[12] states that acute generalized miliary tuberculosis occurs most frequently in babies and young children. In the present series, the peak incidence (Table 1) was found in the third decade. In contrast is the peak incidence of nonmiliary forms of tuberculosis at the Boston City Hospital, which, surprisingly enough, was in the seventh decade. Our findings are not necessarily at variance with the statements by Hartwich and by Amberson, since no children were included in this series. Among adults, however, the disease was more frequent in the younger than in the more advanced age groups.

It is of interest to note that although peak incidences occurred as indicated, acute generalized miliary tuberculosis is by no means unknown in the seventh, eighth and ninth decades. Thirteen per cent of Hartwich's and 14 per cent of Braun's[12] patients were over sixty years of age. Thirty per cent of our patients were over that age, and 16 per cent were over seventy years of age. The oldest patient was eighty-five and the youngest nineteen.

Table 1. *Age Incidence of Acute Generalized Miliary Tuberculosis and of Nonmiliary Tuberculosis Among Adults at Autopsy.**

Age	Total Cases with Nonmiliary Tuberculosis		Total Cases with Miliary Tuberculosis	
yr.	no.	percentage	no.	percentage
15–19	2	—	2	3.2
20–29	10	4.5	13	20.6
30–39	24	9.7	7	11.1
40–49	39	15.8	11	17.5
50–59	46	18.6	11	17.5
60–69	55	22.0	9	14.3
70–79	46	18.6	9	14.3
80–89	10	4.5	1	1.5
90 and over	1	—	0	—
Unknown	14	5.5	0	—
Totals	247		63	

*Chi square = 23.0, when N = 5. P = less than 0.01.

Clinical Aspects

Diagnosis

In this series the ante-mortem and post-mortem diagnoses of tuberculosis were as given in Table 2.

Table 2. *Clinical Diagnosis and Findings at Autopsy.*

Diagnosis	Diagnosed Clinically	Found at Autopsy
Fibrocaseous pulmonary tuberculosis	36	45
Acute generalized miliary tuberculosis	16	63
Tuberculous meningitis	7	7
Tuberculosis of larynx and pharynx	6	2
Tuberculous cervical adenitis	5	–
Tuberculous peritonitis	4	4
Tuberculosis of gastrointestinal tract	4	27
Tuberculosis of bone	2	4
Tuberculous pericarditis	2	4
Tuberculosis of epididymis	1	4
Tuberculosis of kidney	1	6
Tuberculosis of testicle	1	1
Tuberculous panserositis	1	1

In this hospital, the larynx, pharynx and cervical lymph nodes are not routinely examined at autopsy, so that figures for these sites are probably artificially low. The large discrepancy between the clinical and the pathological diagnosis of gastrointestinal tuberculosis is probably due to the obscurity and relative unimportance of the associated symptoms.

As shown, the ante-mortem diagnosis of miliary tuberculosis was made in 16 of the 63 cases (25 per cent), and 2 additional cases were tentatively so diagnosed. A survey of these 16 cases disclosed that the majority were diagnosed on the basis of x-ray examination of the chest. Several cases, however, were apparently diagnosed largely on the basis of the clinical course, the presence of known chronic tuberculosis and the leukocyte picture. Our diagnostic average compares rather unfavorably with that reported by Lewison,[5] who apparently found that 75 (78 per cent) of the 96 cases of acute generalized miliary tuberculosis demonstrated at autopsy at Cook County Hospital were diagnosed clinically.

History and Symptoms

A history of exposure to active tuberculosis was obtained in 16 per cent and a history of previously active tuberculosis in 26 per cent of the 35 cases in which specific inquiry was made.

Anorexia, weight loss and cough were the most prominent symptoms, occurring in 90, 85 and 82 per cent, respectively. Night sweats, dyspnea, chest pain and hemoptysis were recorded in 79, 64, 49 and 15 per cent, respectively. Any or all of these symptoms may occur in fibrocaseous pulmonary tuberculosis without miliary dissemination and did not, for this reason, serve to establish the correct diagnosis in any of our cases. In several cases, however, the rapidity of onset and the severity of symptoms appear to have been of assistance in arriving at the correct diagnosis. Dyspnea was not significantly more frequent in the group of cases that showed massive involvement of the lungs by the miliary process than it was in the group that did not. Hemoptysis was seen in 6 cases of the entire series, and in 5 of these chronic pulmonary lesions as well as miliary involvement of the lungs were present at autopsy. Cough was equally prominent in both groups. Pronounced dyspnea was usually seen as a terminal finding but apparently provided little or no specific diagnostic assistance.

Seven patients presenting neurologic signs and symptoms were diagnosed clinically as having tuberculous meningitis, and the diagnosis was confirmed at autopsy in all. This incidence (11 per cent) is lower than that reported by most authors, probably because children were excluded. It is generally agreed that the more children included in any series, the higher the incidence of tuberculous meningitis.[3, 11, 14]

Physical Findings

Physical findings in acute generalized miliary tuberculosis are seldom of much diagnostic assistance. In many of these cases, physical examinations were necessarily cursory and incomplete, and in only 1 case was a physical finding diagnostic (see below).

The course of the temperature in the disease was described by Cornet[11] as having no definite form and showing irregularity as its most characteristic feature. Hegler[3] found true hectic fever of the so-called "picket-fence" type and continued typhoidal fever in some of his cases, but stated that the irregular remittent type was the most frequent. The latter type is characterized by irregular and unpredictable rises of temperature to 102 or 103° F. every few days, the temperature falling to lower but not to normal values between rises. Afebrile cases are described by most writers, and are said in the older literature to occur most frequently when such complications as tuberculous meningitis, cardiac insufficiency or extreme age are present. After a careful survey of the temperature charts in this series we find ourselves in complete agreement with Cornet. We could find no feature that was common to the entire group, and many of the charts were so irregular as to defy classification, although about one third of them fit roughly into the irregular remittent category. True "picket-fence" charts were noted in 4 cases, and typus inversus charts in 3. The highest temperatures in the entire series were found in one of the cases of typus inversus temperature, the maximum reading being 107°F. All 7 of the cases in which tuberculous meningitis was found showed elevated temperatures, and no such depression of temperature as has been frequently described in the past was found in the group.

Rapid *pulse rates* were the rule, and tachycardia out of all proportion to the temperature was seen in many cases. Sixty per cent of the patients had sustained pulse rates of 120 or higher, and terminal elevations to 160 in association with terminal tachypnea were frequent.

A pronounced increase in the *respiratory rate* has been thought to indicate diffuse miliary involvement of the lungs.[3] An attempt to correlate rapid respiratory rates with miliary involvement of the lungs in this series met with complete failure, and we doubt that the segregation of a clinical group as pulmonary miliary tuberculosis on the basis of marked increase of respiratory rate is justified. Sustained elevations of the respiratory rate to 30 or higher were present in 60 per cent of the series, and terminal tachypnea associated with cyanosis was present in almost all the patients.

The *general appearance* of most of the patients was consistent with that seen in any acute febrile illness. The state of nutrition on entry to the hospital was given as poor in 62 per cent, good in 25 per cent and excellent in 8 per cent. It is interesting to note that several patients were frankly obese but lost weight rapidly during the relatively short course of the disease.

Clubbing of the fingernails was noted on physical examination in 4 cases, 2 of which showed fibrocaseous pulmonary tuberculosis, on which pulmonary miliary involvement was superimposed. In the other 2 cases the lungs at autopsy showed miliary lesions but no chronic tuberculous involvement, suggesting that clubbing is not necessarily dependent on chronic pulmonary changes but may be produced by acute miliary involvement of the lung alone.

Ophthalmoscopic examination disclosed the presence of miliary tubercles of the ocular fundi in 1 case. This observation represents the only physical finding in the series that was diagnostic of acute generalized miliary tuberculosis. Several authors, including Litten,[9] state that miliary involvement of the ocular choroid is a frequent occurrence. Choroidal tubercles are said to be bilateral and to appear as pale, grayish-white oblong patches with indistinct edges. In the early stages, the di-

ameter of such tubercles seldom exceeds 1 mm. When caseation takes place, a central depression may develop in the lesion.[3] Although such tubercles may be confused with other ophthalmoscopic findings, their presence is said to be pathognomonic of acute generalized miliary tuberculosis. We are not able to comment further on this important phenomenon, since few adequate ophthalmoscopic examinations were carried out.

Pulmonary findings consistent with the diagnosis of chronic pulmonary tuberculosis, usually apical in location, were reported in 36 cases. In 29 of them the disease was found at autopsy as diagnosed clinically. Of the 63 cases in the series, 18 were found at autopsy to show miliary involvement of the lungs in the absence of chronic pulmonary tuberculosis. No chest signs of any type were found on physical examination in 4 cases, diffuse fine tomedium rales were found in 6, and various other nondiagnostic signs were encountered in the remaining 8 cases.

Enlargement of the *spleen* has been frequently reported in the literature as occurring in acute generalized miliary tuberculosis. Litten[9] found a palpable spleen in 70 per cent of his cases. Hegler[8] states that splenomegaly in the disease is frequent but that gross enlargement of the spleen is extremely rare. Amberson[12] holds that the spleen is palpable in a minority of cases. It is generally recognized that enlargement of the spleen at autopsy does not necessarily mean that the organ was palpable during life. In addition to the weight of the spleen, its palpability depends on other factors, including the experience of the examiner, the thickness of the abdominal wall and the degree to which the patient is able to co-operate. Obviously a spleen that is greatly enlarged by weight may not be palpable clinically if other factors are not favorable. We believe that a spleen weighing over 400 gm. should be palpable clinically, particularly if careful and repeated examinations are carried out. Under optimal conditions, spleens weighing considerably less may also be palpable. Abdominal palpation was reported in 49 cases. The spleen was described as palpable in 6 cases (12 per cent), and in 5 of these it was enlarged by weight (over 195 gm.) at autopsy. The largest spleen in the group weighed 1300 gm. and contained many tuberculomas in addition to miliary tubercles. Although 47 per cent of the spleens in this series weighed over 195 gm. at autopsy, only 4 (7 per cent) weighed over 400 gm., so that marked enlargement was rare both at physical examination and at autopsy.

Enlargement of the *liver* as a result of involvement in miliary tuberculosis is not usually described. Clinically, 35 per cent of these patients were reported to show palpable livers, but significant enlargement at autopsy was reported in only 6 per cent. In no case was it possible to demonstrate that hepatomegaly was due to miliary involvement of the liver per se.

Accumulation of serous fluids in amounts generally considered to be abnormally large was found at autopsy in many cases. Pleural fluid in amounts varying from 150 to 4900 cc. was found at autopsy in 19 cases (30 per cent) but was detected clinically in only 5 cases (8 per cent). Two cases in which no chronic tuberculosis of the lungs or pleura was found but in which diffuse pulmonary miliary tuberculosis was present showed significant amounts of fluid in the pleural spaces. Nine cases (14 per cent) showed abnormally large amounts of pericardial fluid at autopsy. In 5 of these, the amounts were relatively small, — from 50 to 75 cc., — and there were no symptoms during life attributable to the accumulation of fluid. In the other 4 cases, there was 150 to 800 cc. of pericardial fluid at autopsy. Two of these patients showed caseous tuberculous pericarditis before death. Miliary tubercles were found at autopsy in the pericardium in 2 cases, but in neither was there an abnormal increase in pericardial fluid. From 200 to 1500 cc. of intraperitoneal fluid was reported at autopsy in 4 cases (6 per cent), and the fluid was found clinically in 1 case.

Length of Hospital Stay and Duration of Disease

The shortest hospital course was twelve hours, and the longest was two hundred and twenty-five days. Seven patients died after being in the hospital for thirty-eight hours or less, and 6 remained there for three months or more. Most of the patients were in the hospital for two to four weeks. The length of the hospital stay and the duration of the disease are not, of course, necessarily synonymous. Most patients appeared to have developed the acute illness outside the hospital and to have sought hospitalization only when their symptoms became extremely severe. A few patients seem to have developed the condition while in hospital, and 1 patient suffered recurrent acute episodes, probably due to repeated miliary disseminations. In determining the apparent duration of the acute generalized miliary disease, such information was utilized as the onset of acute symptoms, the onset of febrile episodes, the changes in the leukocytes and x-ray information. Eighty-three per cent of the patients died two months or less after the apparent onset of acute symptoms, and the average duration of the illness was five and a half weeks. The shortest course in the series was five days in length, and the longest thirty-two weeks.

Hematologic Findings

Leukocytes

Adequate descriptions of leukocytic reactions in acute generalized miliary tuberculosis appear in the literature with some rarity. Warthin[15] reported 2 cases in 1896 in which prolonged leukopenia and elevated percentages of neutrophils were found. As long ago as 1905, Arneth[16, 17] pointed out that in this type of tuberculosis, as in the experimental

disease produced in animals by the intravenous injection of tubercle bacilli, it is the neutrophil that is most actively involved in the leukocytic reaction of the organism to the infection. He placed the emphasis on excessive demand for neutrophils rather than on defective supply in explaining the leukocytic changes. More recently, Medlar[18] and Muller[19] have expanded Arneth's views and have also directed attention to the important role of the neutrophil in tuberculous infection and to the demand made by local tuberculous lesions for such cells. The effects on the peripheral blood picture of such a demand seems to depend largely on the ability of the bone marrow to keep up with requirements. Thus, in any type of tuberculosis, if developing lesions make excessive demand for neutrophilic cells on the bone marrow, leukopenia may result. On the other hand, bone-marrow response may be sufficient from time to time to produce frank leukocytosis. In either case many young neutrophils reach the circulating blood and the tendency for the count to shift to the left is more or less marked. That overwhelming infection, including tuberculosis, can at times produce what appears to be bone marrow depression is well known. There is no positive evidence, however, that the mere presence of miliary tubercles in the marrow can per se exert a depressant effect. In metastatic involvement of the marrow by neoplastic disease, Vaughan[20] found that the actual space occupied by neoplastic tissue was insufficient to account for the observed decrease in marrow function. Similarly, in none of our cases was there sufficient involvement of the bone marrow to allow explanation of peripheral blood changes on the basis of mechanical depression of marrow function. Interesting in this connection is the experimental work done by Doan and Sabin,[21] who produced extensive lesions of the bone marrow in rabbits by intravenous injection of virulent tubercle bacilli. The result was initial depression of marrow function as judged by peripheral blood observations, followed in the animals that survived by compensatory hyperactivity of the marrow and finally by functional and morphologic recovery.

The increase in percentage of neutrophils and the more or less marked shift of the Arneth count to the left were stated by Arneth to be of definite prognostic and diagnostic value. Medlar[18, 22] considers, on the basis of numerous clinical observations, that in tuberculous patients an increase in the percentage and absolute number of neutrophils, whatever the total leukocyte count, is indicative of a progressive process. Such changes are not limited to acute generalized miliary tuberculosis but may be present in active pulmonary and other forms of active tuberculosis as well.

Our observations are based on 49 of the entire series of 63 cases. Eleven of the total number were excluded because of the presence of significant nontuberculous infection at autopsy, 2 because no blood counts were available, and 1 because of the presence of chronic myelogenous leukemia. So far as could be ascertained at autopsy, the 49 remaining cases showed no disease apart from the tuberculous infection that might have affected the blood picture.

Total leukocyte counts in the 49 cases were distributed as follows: in 24 cases (49 per cent) there was leukopenia (a total leukocyte count of less than 5000) at some point during the hospital course; in 14 cases (29 per cent) there was leukocytosis (a count of 10,000 or more) at some point during the hospital course; and in 16 cases (33 per cent) the total leukocyte counts were within the normal range. The highest total count was 20,700, and the lowest 1600.

In 11 of the 24 cases showing leukopenia at some time during the hospital course, the total leukocyte counts were persistently lower than normal for two weeks or more, the longest period of leukopenia being twenty weeks. In 6 cases, leukopenia, leukocytosis and normal total leukocyte counts were all observed. Seven patients showed leukopenia on entry but died before further observations could be made.

Differential leukocyte counts, like the total counts, varied in individual patients from time to time. A total of ninety differential counts was available in 35 of the 49 cases. Increased percentages of neutrophils, along with decreased percentages of lymphocytes, were observed in 31 cases (89 per cent). Immature neutrophils were extremely frequent, and in several cases the immature forms outnumbered the mature forms. In 4 cases there was an increased percentage of lymphocytes with a normal or slightly low percentage of neutrophils. Persistent monocytosis was not present in any case, although a slight increase in the percentage of monocytes was seen in thirteen of the ninety differential leukocyte counts available.

Of the 24 cases showing leukopenia, differential counts concomitant with low total leukocyte counts were available in 18. Fifteen of the 18 (83 per cent) showed an increase in neutrophilic elements, the highest percentage observed being 96. Immature neutrophils up to 25 per cent were observed in this group. Although 2 of the cases showing leukopenia also showed a slight decrease in neutrophilic elements, in none was there a picture consistent with or suggestive of granulocytopenia.

The combination of leukopenia and relative neutrophilia was striking. Although this combination, as indicated by Sturgis,[23] is not limited to acute generalized miliary tuberculosis, it may be of diagnostic assistance. In typhoid fever, for example, the leukopenia is usually associated with relative lymphocytosis at the expense of neutrophils, and in true agranulocytic conditions the leukopenia is marked by extreme diminution of neutrophils and less marked diminution of lymphocytes.

Bone-marrow sections were made at autopsy in 37 of the 49 cases, and 33 of these contained miliary tubercles. The bone marrow in 19 of the 24 cases with leukopenia was involved by the miliary process and was uninvolved in 2 cases. No sections were available in the remaining 2 cases. In 9 of the 14 cases with leukocytosis, the marrow contained miliary tubercles; in 1 of the group no tubercles were present, and in 4 no sections were available. It is not surprising that no correlation between the hemopoietic activity of the marrow at the time of death and the blood picture during life could be established in the series. With regard to hemopoietic function, the bone marrow appeared normal or hyperactive in the overwhelming majority of cases, and definite hypofunction was noted in only 2 cases.

TABLE 3. *Summary of the Blood Findings in a Patient with Evidence of Myelophthisic Anemia.*

Hospital Day	White-Cell Count	Neutrophils		Lympho-cytes	Mono-cytes	Nucleated Red Cells Per 100 White Cells	Platelets	Hemo-globin (Sahli)	Red-Cell Count	Appearance of Red Cells
		mature	immature							
		%	%	%	%			%	$x10^6$	
1	5400	76		16	8		Decreased	72	3.8	
2	2800	76		20	3		Decreased	70	4.0	Moderate anisocytosis; MCHC, 32.3, and MCV, 83.
3	4400	40	30	17	9	4	119,000	71	3.8	Moderate anisocytosis; polychromatophilia; MCV, 88.7, MCHC, 33.6, and MCH, 26.5.
4	4000	48	27	12	8	4	Markedly decreased			
5	3400							68	3.7	
11	6000	60	14	18	7	3	Decreased	58		Anisocytosis and poikilocytosis
15	3800							61	3.2	
16								60	3.0	
23	4800	86		10	4	3	Decreased	55	2.8	Anisocytosis and poikilocytosis
29	2800							62		
32	6100						96,000	43	2.2	
37	5000	70		18	10	12	Decreased	46	2.3	Marked variation in size and shape; polychromatophilia.
42	5400							50	2.2	
49	8500	66		31	3	10		52	2.3	

Hemoglobin and Red Cells

The occurrence of anemias of various types in pulmonary tuberculosis is discussed at length by Muller.[19] Hegler[3] gives the range of hemoglobin determinations and red-cell counts in acute generalized miliary tuberculosis as 65 to 85 per cent and 3,500,000 to 4,500,000, respectively. Both Hegler and Wintrobe[24] state that severe anemias in tuberculosis are rare.

In this series, 46 patients had both hemoglobin determinations and red-cell counts. Moderate normochromic anemia was seen in 39 (84 per cent). The lowest hemoglobin value and red-cell count were 43 per cent (Sahli) and 1,840,000, respectively. The vast majority of the determinations were well within the range given by Hegler.

Concomitant Depression of Blood Elements

The occurrence of a condition resembling so-called "aplastic anemia" in acute generalized miliary tuberculosis was noted by Dyke[25] and by Rosenthal,[26] the latter placing special emphasis on the decrease in platelets and the resulting hemorrhagic diathesis. Arneth[27] reported extremely low platelet counts in 6 cases of this type of tuberculosis, all of which showed leukopenia and neutrophilia in addition. Two of our cases showed blood findings quite similar to those in Arneth's cases. The following points were common to both: moderate to severe leukopenia, with occasional normal or elevated total leukocyte counts; an increase in percentage of neutrophils; decreased platelets; normocytic or slightly microcytic anemia; and polychromatophilia. In addition, 1 case (Table 3) showed abnormal numbers of nucleated red cells and increased numbers of immature neutrophils in the peripheral blood, findings consistent with the condition known as myelophthisic anemia and ordinarily associated with space-occupying lesions of the bone marrow. At autopsy the bone marrow contained relatively few miliary tubercles and showed markedly increased cellular density. There were signs of increased activity in both the erythrocytic and leukocytic series.

The second case of this general type in the early days of the hospital course showed a peripheral blood picture suggestive of an aplastic state. Blood studies done during this period all showed anemia, leukopenia and thrombocytopenia, and except for a slight to moderate increase in the percentage of polymorphonuclear cells, there was little peripheral evidence of compensatory activity on the part of the bone marrow. Subsequently there was steady improvement in the leukocyte picture, and when the patient died, four weeks after entry, a frank leukocytosis was in evidence. The appearance of the marrow at autopsy was in keeping with the findings in the peripheral blood in that there was increased granulopoiesis but decreased erythropoiesis. Miliary tubercles were present but were few in number.

Pathology

Pathogenesis

Since the original descriptions of acute generalized miliary tuberculosis by Bayle[28] and Laennec,[29] there has been considerable controversy concerning the pathogenesis of the disease. Much of this material has recently been reviewed by Auerbach.[8]

It has long been apparent that miliary disseminations are ultimately blood-borne. The condition is generally attributed to the release of relatively large numbers of tubercle bacilli, directly or indirectly, from a chronic focus, and it is about such foci that most of the controversy has centered. Laennec recognized a connection between a chronic tuberculous focus and miliary dissemination of the disease, a concept that was elaborated in some detail by Buhl[30] in 1858. On the basis of autopsy findings, Weigert[31] concluded that the disease stems from erosion and penetration of veins by extravascular tuberculous foci. Benda[32] agreed in principle but suggested that tubercles of the venous intima, developing as a result of the lodging of a single bacillus or of several bacilli from the circulating blood, were ultimately responsible for the overwhelming release of organisms, resulting in acute generalized miliary tuberculosis. That a tuberculous lesion of the thoracic duct may initiate such a condition has also been postulated, and Hartwich[10] states that such a lesion was apparently the origin of the miliary dissemination in 26 per cent of his cases. It appears from Auerbach's observations that chronic tuberculous foci, developing in lymphatic channels draining an infected area, ultimately break down and release tubercle bacilli into the venous circulation by way of the thoracic duct. This view is attractive from the anatomic standpoint, and it has in its favor the very extremely frequent involvement of lymph channels and lymph nodes draining chronic tuberculous foci.

Weigert's[33] tenet that chronic pulmonary tuberculosis renders the patient more or less immune to miliary disseminations can no longer be seriously considered. Auerbach's findings, as well as our own, are in complete disagreement with Weigert's statement on this point, since chronic pulmonary lesions were present in 64 per cent of his series and in 71 per cent of our own. Reisner[34] indicated the importance of chronic extrapulmonary foci, such as bone and genitourinary lesions, in the production of acute miliary disseminations, but in our series such foci were decidedly less frequent than pulmonary foci. Chronic pulmonary foci may give rise to chronic extrapulmonary foci, which in turn may originate acute miliary disseminations, and it is usually impossible to decide at autopsy which of the chronic foci was responsible for the acute episode.

A sudden release of large numbers of tubercle bacilli into the blood stream, whatever the site of origin, does not necessarily result in immediately fatal disease. One of Auerbach's cases had four separate seedings of the lungs over a period of fifteen months, as demonstrated by x-ray and confirmed at autopsy. If, however, the number of organisms is large and the patient is unusually susceptible, the spectacular condition known as sepsis tuberculosa acutissima is said to occur. This condition is usually described as an extremely acute and generalized process that results in death before miliary tubercles have had time to form. At autopsy, small areas of necrosis containing numerous tubercle bacilli but provoking little or no cellular reaction are found scattered throughout the body. In addition to our 63 cases of acute generalized miliary tuberculosis, we noted 2 cases of chronic, healed miliary tuberculosis in which several disseminations had apparently occurred. No cases were found that could be classified as sepsis tuberculosa acutissima.

Criteria for Pathological Diagnosis

The establishment of suitable criteria for the pathological diagnosis of acute generalized miliary tuberculosis is far from easy. Our studies of the literature have failed to disclose any criteria that were entirely satisfactory. In practice, pathological diagnosis of cases in which the disease is truly overwhelming is not difficult. The difficulty arises when one attempts to decide just how generalized miliary involvement must be before a case may be labeled as acute generalized miliary tuberculosis. Clearly, the discovery of isolated miliary tubercles in a single organ does not justify the diagnosis, nor does the finding of numerous chronic but generalized lesions.

In selecting cases for a study of this type, one is unfortunately forced to establish definite criteria, even though dividing lines between various types of the disease are far from definite. We considered it essential to take the term "acute generalized miliary tuberculosis" literally so far as possible and made the following requirements for the pathological diagnosis: that the tubercles be acute, provoking little or no fibrous tissue reaction; that the disease be generalized sufficiently to involve the liver, spleen and at least one additional tissue, such as lung, bone marrow or kidney*; and that the tubercles conform, with regard to size, to the miliary description.†

Chronic Foci

The distribution of chronic tuberculous foci in this series is shown in Table 4. Chronic foci were found in 60 cases (95 per cent). The chronic lesions found in 45 of the cases (71 per cent) were all instances of fibrocaseous pulmonary tuberculosis. Intestinal lesions, present in 27 cases (43 per cent), were without exception chronic tuberculous ulcerations, and in 1 case the ulcerative process had pro-

*Three cases were included in which sections of liver or spleen were not available; numerous acute tubercles in four or more tissues other than these organs, however, were demonstrated.

†The size of the tubercles varies considerably, although most of those in our cases were 3 mm. or less in diameter.

duced a spontaneous ileocolostomy. Distribution of the ulcerative lesions through the various portions of the intestine is shown in the table.

Chronic caseous lesions of lymph nodes were found in 37 cases (59 per cent). Infrequent examination of the thoracic duct probably accounted for the fact that this structure was found to be involved by chronic tuberculous lesions in only 4 cases.

Tuberculosis of the genitourinary tract, including the kidney, prostate, seminal vesicles, epididymis and testicles, occurred in 14 cases (22 per cent). Three cases in this group also showed tuberculous meningitis, a finding apparently not in keeping with the frequent relation between tuberculous meningitis and tuberculosis of the genitourinary tract described by some authors.[6, 7]

Chronic lesions of the cardiovascular system were seen in 5 cases. In 1 case, a caseous lesion of the tip of the right auricular appendage, measuring 0.9 by 0.5 cm., was found to have ulcerated through to the endocardial surface, at which point there was a small mural thrombus. Chronic lesions were found in the pulmonary vascular system in 3 cases — in the pulmonary artery in 2 and in a small branch of the pulmonary vein in 1. One of the lesions of the pulmonary artery took the form of a verrucous arteritis, and a fungating gray mass, approximately 0.7 cm. in diameter, was found attached to the intima 1 cm. above the pulmonary valve. Microscopically, the lesion contained numerous tubercle bacilli and cellular débris enmeshed in a fibrin network. Finally, there was 1 case of intimal tuberculosis of the ovarian vein.

TABLE 4. *Distribution of Chronic Tuberculous Foci.*

LOCATION	NO. OF CASES		PERCENTAGE
Lungs		45	71
Lymph nodes:		37	59
Tracheobronchial	26		
Mesenteric	14		
Abdominal	3		
Digestive tract:		27	43
Esophagus	1		
Jejunum	7		
Ileum	23		
Colon	23		
Appendix	1		
Rectum	4		
Genitourinary tract:		14	22
Kidneys	6		
Prostate	6		
Epididymes	4		
Testicles	1		
Seminal vesicles	2		
Adrenal glands		6	10
Spleen		6	10
Brain		5	8
Cardiovascular system:		5	8
Heart	1		
Pulmonary arteries	2		
Pulmonary veins	1		
Ovarian vein	1		
Pericardium		4	6
Peritoneum		4	6
Bones		4	6
Thoracic duct		4	6
Pleura		3	5
Liver		1	
Pharynx		1	
Larynx		1	

Miliary Distribution

According to Auerbach,[8] in cases in which miliary seeding is extensive, routine microscopic examination discloses miliary tubercles in almost all parenchymatous organs. Obviously, the number of organs routinely sectioned influences in large measure the apparent distribution of miliary lesions. Since the number of organs routinely examined varies considerably from laboratory to laboratory, many of the reported differences in miliary distribution are fictional.

Litten[9] and most modern writers[5, 8] state that the lungs, liver, spleen, kidney, bone marrow and choroid are always involved in acute generalized miliary tuberculosis and that the voluntary muscles are always spared. Miliary tubercles of the skin have been reported, but this finding appears to be extremely rare.[35]

The miliary distribution in this series is presented in Table 5. The almost invariable involvement of the liver and spleen is well known. Our figures for these organs (100 per cent) may be artificially high, since the cases were selected on the basis of the finding of miliary tubercles in these sites. The extremely frequent involvement of the bone marrow has likewise often been pointed out. In the present series the bone marrow contained miliary tubercles in 84 per cent of the cases. Renal involvement by the miliary process occurred in 51 per cent, and the adrenal glands were diseased in 42 per cent. The latter figure is considerably higher than that found by Lewison et al.[5] Although sections of the pancreas were made in only 25 cases, it is noteworthy that miliary involvement was found in 5 cases, a rather high incidence according to previous reports. Meningeal involvement was lower than is generally re-

TABLE 5. *Distribution of Miliary Tubercles.*

LOCATION	NO. OF CASES EXAMINED	CASES SHOWING TUBERCLES NO.	PERCENTAGE
Spleen	60	60	100
Liver	61	61	100
Bone marrow	50	42	84
Lungs	63	49	63
Kidneys	60	32	53
Adrenal glands	45	19	42
Testicles	12	5	41
Ileum	9	3	33
Meninges	24	7	29
Pancreas	25	5	20
Brain	24	3	12
Heart	39	4	10
Tracheobronchial nodes		13	—
Abdominal nodes		7	—
Peritoneum		7	
Mesenteric nodes, urinary bladder, pleura, omentum, pericardium, jejunum and fallopian tubes		2 (each)	—
Epididymis, gall bladder, seminal vesicle, ureter, thoracic duct, duodenum, endometrium, ependyma, appendix, colon, pituitary gland, parathyroid gland and cervical node		1 (each)	—

ported; reasons for this discrepancy have already been mentioned. Miliary tubercles have often been noted in the thyroid gland, but in none of these cases was the gland examined. For the same reason, the frequency of involvement of the ocular choroid could not be determined.

Discussion

From a practical point of view, more accurate diagnosis of acute generalized miliary tuberculosis is desirable for two reasons: first, the prognosis in the disease is considerably worse than that in most other forms of tuberculosis and may influence the physician's management of the case; second, more careful and detailed observations before death, particularly in the laboratory, may yield information of general value in tuberculosis.

The history often supplies no information of value, but may disclose either previous significant exposure to tuberculosis or the existence of chronic tuberculous infection. The incidence of acute generalized miliary tuberculosis among adults, particularly among those suffering from fibrocaseous pulmonary tuberculosis, was higher in this series than has generally been reported.

The course of the temperature is usually extremely irregular and is of little or no help in arriving at the correct diagnosis. More or less marked, sustained elevations of the respiratory and pulse rates may usually be expected. Although classification of cases of the disease into pulmonary and typhoidal types on the basis of temperature, pulse and respiratory charts figures prominently in the older literature, we doubt the justification for or clinical importance of such classification.

On physical examination, actual observation of miliary tubercles is possible only by ophthalmoscopic examination. We believe that a considerable number of our cases would have been correctly diagnosed before death had careful and repeated ophthalmoscopic examinations been carried out. Pulmonary findings in this series either were those of chronic pulmonary tuberculosis or were equivocal. Splenomegaly on physical examination occurred so infrequently that it was of relatively little diagnostic assistance. Spleen weights at autopsy sustained the finding at physical examination that pronounced splenomegaly in the disease is infrequent.

Among laboratory procedures the diagnostic importance of x-ray examination of the chest is fully established and needs no further comment. The importance of biopsy of the bone marrow as a laboratory procedure in the diagnosis of the condition was evidently not fully appreciated by the physicians in charge of our cases. Schleicher[36] has recently laid proper emphasis on this point and has described a method by means of which tubercles may be visualized in material obtained by marrow aspiration instead of biopsy. In view of the frequent involvement of the marrow at autopsy, it is apparent that a definite ante-morten diagnosis may be reached by ante-mortem examination of the marrow, a procedure that should certainly be resorted to in suspicious cases.

Serial examinations of the red and white cells appear to be of considerable diagnostic assistance, but isolated examinations are probably misleading as often as they are helpful. The most constant change in the leukocytic picture seems to be an increase in the percentage of neutrophils and a shift of the Arneth count to the left. These changes may be present whatever the total leukocyte count, but their diagnostic value is enhanced if they are found in association with leukopenia. None of these changes are specific for acute generalized miliary tuberculosis. When they are seen in patients known to be suffering from a chronic form of tuberculosis, the condition should be considered. If such a disturbance of the leukocytic picture develops in cases of obscure, febrile illness in which no specific bacterial agent is demonstrable, the disease should rank well up among the diagnostic possibilities.

Peripheral depression of several blood elements concomitantly, including leukocytes, red cells and platelets, is consistent with the diagnosis of acute generalized miliary tuberculosis but was not frequent in this series.

The chronic focus from which acute generalized miliary tuberculosis originates in a given case can seldom be definitely identified, but in the light of recent reports and of our own findings, we believe the lymphovenous route to be the likeliest one in the majority of cases, if not all. Chronic tuberculous lesions often develop in lymph nodes and channels draining an infected area. From this point, tubercle bacilli may easily enter the venous blood by subsidiary lymph channels and the thoracic duct. The latter structure may itself become incidentally infected, and less frequently it is involved from without by adjacent chronic lesions.

Many questions with regard to the distribution of miliary tubercles in acute generalized miliary tuberculosis remain unanswered. The frequent involvement of such sites as the liver, spleen, lungs and bone marrow is well established, but knowledge of the frequency of involvement of certain other sites is incomplete. Routine microscopic examination at autopsy of the ocular choroid, thyroid and pituitary glands, pancreas and adrenal glands in suspected cases would doubtless provide many of the answers not yet available. Our findings suggest that the adrenal glands and pancreas may be somewhat more frequently involved by the miliary process than is usually reported.

Conclusions

The general incidence of acute generalized miliary tuberculosis at autopsy among adults at the Boston City Hospital from 1937 to 1941, inclusive, was 1.55 per cent. The incidence of the condition among cases

of tuberculosis of all types at autopsy for the same period was 20.3 per cent.

Although chronic pulmonary tuberculosis was diagnosed fairly accurately in this series, the clinical diagnosis of acute generalized miliary tuberculosis was achieved in only 25 per cent of the cases. The history and physical findings were of limited diagnostic assistance, x-ray examination of the chest and the clinical course being much more important in this respect. The only direct means of visualizing the miliary tubercles during life — namely, by ophthalmoscopic examination and bone-marrow biopsy — were grossly neglected in this series.

Splenomegaly was observed on physical examination in 6 cases (12 per cent), and the finding was confirmed at autopsy in 5. The spleen weighed over 195 grams at autopsy in 47 per cent of the cases, but enlargement by weight was marked (over 400 gm.) in only 7 per cent. The average duration of life after apparent onset of the disease was five and a half weeks, the shortest course being five days and the longest thirty-two weeks.

Increased percentage of neutrophils and shift of the Arneth count to the left were present in 89 per cent of the 35 cases in which differential counts were made. Leukopenia was frequently seen but was by no means the rule.

Chronic tuberculous lesions were found in 95 per cent of the series. The lung was the site most frequently involved, being affected in 71 per cent.

The organs most frequently involved by miliary lesions were the spleen, liver, bone marrow, lungs, kidneys and adrenal glands. Some of the difficulties in establishing the frequency with which a given organ is involved by the miliary process are discussed.

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THE LATE RESULTS OF FEMORAL THROMBOPHLEBITIS AND THEIR TREATMENT*

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THERE is probably an advantage, in these recent days when thrombosis in the veins of the lower limbs is receiving active treatment by surgical procedures as well as by anticoagulants, in visualizing the usual end stage of the disease untouched by such methods. It is as yet too soon to learn how much or how little they alter its natural course, even supposing that in any considerable proportion of cases their use is attempted, for when one considers that venous thromboses occur in association with injuries, operations, childbirth and serious cardiac and other diseases, as well as spontaneously in everyday life, it is probable that in most instances today, the disease still has an opportunity to reach its full development.

In the light of present-day researches, culminating in the clinical observation of Bauer[1] and the pathological studies of Hunter and his associates,[2, 3] it is clear that most venous thromboses begin below the knees. Undoubtedly they are then able to pursue a variety of courses, the nature of which has often been pointed out.‡ But how many undergo spontaneous cure, how many retain their character of soft thrombi likely to cause pulmonary embolism, and how many develop into the familiar, obstructive femoroiliac thrombophlebitis is unknown. Certainly an obstructive, inflammatory thrombosis is the late stage toward which all such processes tend, and it is highly probable that it is by far the most frequent end result of all venous thrombosis in the lower limbs. I shall resist the temptation to show how surgical interruption of the diseased vein or the use of anticoagulants may modify or even prevent this development, and how, in the early stage of an actual thrombophlebitis, lumbar sympathetic block may favorably influence peripheral vasoconstriction and edema. These matters, of course, should sometime be studied in the light of the findings secured by such investigations as the present.

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‡It is difficult to see why a soft and, at first, nonobstructive thrombosis should, in time, if it does not cause either fatal embolism or end in healing by local organization, go over to the obstructive, inflammatory type of disease. But Bauer has followed the process through, by phlebography, and one certainly encounters its earlier stages, as betrayed by nonfatal embolism or local soreness, lameness (with or without swelling) and muscular irritability, before the typical phlegmasia alba dolens sets in. Moreover, the pathological studies of Hunter, Sneeden, Robertson and Snyder and of Hunter, Krygier, Kennedy and Sneeden are consistent with earlier German and Swedish investigations in showing how frequently lower leg venous thromboses can be found in persons dying after confinement to bed by a great variety of diseases. One is thus made to realize that such thrombosis is common as a terminal affair and that it could readily go on to more advanced stages if death did not supervene. Again, Conner's[4] account of prodromal signs in the legs and feet in the typhoidal thrombophlebitis of earlier days is strong evidence for early local lower-leg thrombosis as leading to the full-blown thrombophlebitis. I have attempted, in a recent publication,[5] to picture diagrammatically the various courses that lower-leg venous thrombosis may pursue.

THE GROUPS OF LATE RESULTS

The late results of femoroiliac thrombophlebitis seem to be divisible into five groups, and although some cases present features characteristic of more than one group, most of the 156 that form the basis of this report are easily classified. I have made no attempt to include the many patients I have seen in hospital wards, for these represent almost exclusively the disabling state of ulceration characteristic of Group 2. If included, they would still further enlarge that group.

Group 1. Some degree of edema remains, so that the ankle and lower leg swell during the hours of work or standing, discomfort is unimportant, congestion is not a feature, the skin is healthy, and the edema recedes, or even disappears, overnight. This group is large — how large is difficult to say, since many patients who fall into it make no complaints. I have included my own few cases, both for statistical purposes and for my brief account of treatment, with Group 2, for it is splitting hairs to isolate the mild edemas with negligible cutaneous changes from the serious ones complicated by pigmentation, induration and ulceration.

Since edema is the basic disorder in both groups, this is perhaps the best place to explain that it is likely to be due, not only during but after the acute stage of thrombophlebitis, to several causes — namely, elevated venous pressure, peripheral vasospasm (in the arterioles and venules) and impaired lymphatic drainage. These causes are so often combined that only occasionally is it possible to say that one of them alone predominates.

Group 2. Postphlebitic pigmentation and induration are present, and ulceration, in a variety of forms, often occurs. This group is far larger than any other. I find 95 cases, or 61 per cent, that fall into Groups 1 and 2. Edema is a constant feature. The typical lesion is usually referred to as "varicose ulcer," although varicose veins are seldom associated with it and, even if present, have no causal relation to it.

The characteristic physical signs are cutaneous pigmentation, diffuse induration, local heat and often ulceration, in the lower two thirds of the lower leg, usually on its inner face above the ankle. Sometimes this disorder is most marked near and below the malleoli, the inner rather than the outer. "Varicose eczema" is occasionally seen. There is thought to be present, according to Thompson's[6] interpretation, a vicious circle of edema and sensitization of the tissues to foreign protein absorbed from the feet, toes and nail beds. The antigen is probably retained in the edema fluid for long periods

of time. Actually, it appears to injure the walls of the arterioles, causing extravasation of blood, — hence the pigmentation, — and gives rise to a slow necrosis of fat with scar formation.[6] Ulceration is not a primary feature. The source of the supposed antigen may be a fungus, — Trichophyton, — although in some cases it seems to be bacterial. In occasional cases, varicosity of the saphenous system, secondary to the original thrombophlebitis, contributes to the local disorder.

Group 3. A pain complex becomes established early in the convalescence and irrespective of all other signs. The situation and distribution of the pain have no relation to any of the great nerves. With it are usually associated vasomotor changes in the skin of the affected leg and a stocking-like paresthesia, the whole giving the impression of a functional disorder. This is a fair-sized group, there being 27 cases, or 17 per cent.

Group 4. The leg is the seat of marked venous congestion. The foot and ankle are usually involved, being slightly cyanotic with prominent surface veins. There may be distended veins on the abdominal wall and in the groin. Edema is not necessarily present, nor postphlebitic induration and pigmentation. This is the smallest group — 8 cases, or 5 per cent.

Group 5. Recurrent thrombosis occurs in the deep and, often, the superficial veins. This takes the form of attacks at varying intervals over a period of years. The attacks, because they usually involve veins previously thrombosed and canalized, are less outspoken than the original thrombophlebitis. They are an occasional source of recurrent, and therefore nonfatal, pulmonary embolism. This is a moderate-sized group of 26 cases, or 17 per cent.

Treatment

Although treatment is not of primary concern here, some account of what appear to be appropriate methods of managing the various groups is in order.

Groups 1 and 2. Since edema is the basic difficulty, it is obvious that its relief will cure early, mild cases and will favorably influence late, advanced cases, even though cutaneous and subcutaneous changes are well established.

The relief of postphlebitic edema is best initiated by a few days in bed, with the foot of the bed elevated 4 to 6 inches. Free exercise of the legs, to forward lymphatic drainage, is encouraged. This is a desirable introduction to any specific treatment.

If even a short, continuous stay in bed is impossible, at least the patient can sleep in a bed so elevated and can supplement such gravity drainage during the day by a number of ten-minute periods during which the leg is raised on an inclined plane to an angle of 20 to 30° and gently exercised. When going about or working, the patient should wear a semielastic bandage or elastic stocking from toes to knee, stand as little as possible and avoid sitting with the legs dependent and relaxed.

Hand in hand with the relief of edema goes treatment of the skin, intended to do away with sources of absorbed protein substances, chiefly derived from fungi. The nails must be softened by soaks, accumulations beneath them being gently scraped away. Partly depending on the acuteness or chronicity of such infections, soaks, liquid applications, ointments and powders may be used, a matter calling for expert dermatologic knowledge and technic. It is probably important that local applications should alter the reaction of the skin; in which direction it is not easy to say, but it is perhaps best in the direction of increased acidity.

Actual ulceration brings up the problem of secondary infection, possibly by anaerobic or facultative anaerobic bacteria, and calls for bacteriologic studies and the internal as well as the external administration of appropriate drugs. Only the ulcer not chronically infected will be cured by relief of edema and venous stasis alone. Should varicose veins be present, section or, rarely, excision should be used to relieve back pressure. Sclerosing injections seem always to do harm, in that they increase the local inflammatory reaction. Radical resection and skin-grafting of the diseased tissues should only occasionally be used.

Group 3. This group is characterized, as I have pointed out in an earlier publication,[7] by a pain complex, and is distinguishable only by a history of thrombophlebitis from the "minor causalgia" that occasionally follows injury. It is, however, rather more responsive to treatment, and its identification is not difficult. The pain is "bursting" or "throbbing" or radiates down the center of the leg, being brought on, equally often, by exercise or long standing. The leg usually appears a little enlarged and, as a whole, faintly cyanotic, although dilated veins are absent. Below the knee, the skin is slightly "numb," — that is, dull to pinprick, — but distribution of the numbness does not follow the fields of the sensory nerves. Squeezing the calf, as by a blood-pressure cuff, is very disagreeable. The peripheral pulses in the foot are sometimes diminished, — one of them may even be absent, — suggesting some degree of constriction of the large arteries.

Probably this state is residual from the vasomotor disorder of the acute stage of thrombophlebitis, for it is almost invariably relieved, for the moment at least, by sympathetic lumbar block. Successive reinforcing blocks prolong the period of relief and usually effect a cure. In late and obstinate cases, sympathectomy is required.

Group 4. This group, comprising the cases presenting venous congestion, yet with little or no edema, is one from which surgery has in the past been held to be barred, apparently on the ground that all distended veins, visible or invisible, are still capable of carrying blood uphill and must not be disturbed. This attitude should decidedly be recon-

sidered; no valveless veins draining the lower limbs—except the iliac veins and vena cava — are capable of forwarding blood against gravity, and since the column of blood they contain transmits high back pressures on lifting, straining and coughing, their interruption must always benefit and can never harm the venous return. Moreover, the blood that accumulates in, and even flows down, these veins must be carried by collateral vessels, which do the back pressure. The canalization of thrombosed vessels is well known to pathologists, a process that I have illustrated in the accompanying diagrammatic sketches (Fig. 1). The conditions pictured have actually been noted at operation. It would have been better if the veins had remained plugged, as Bauer,[8] on phlebographic grounds, holds to be the rule.*

With these matters in mind, the femoral and saphenous systems of the congested postphlebitic

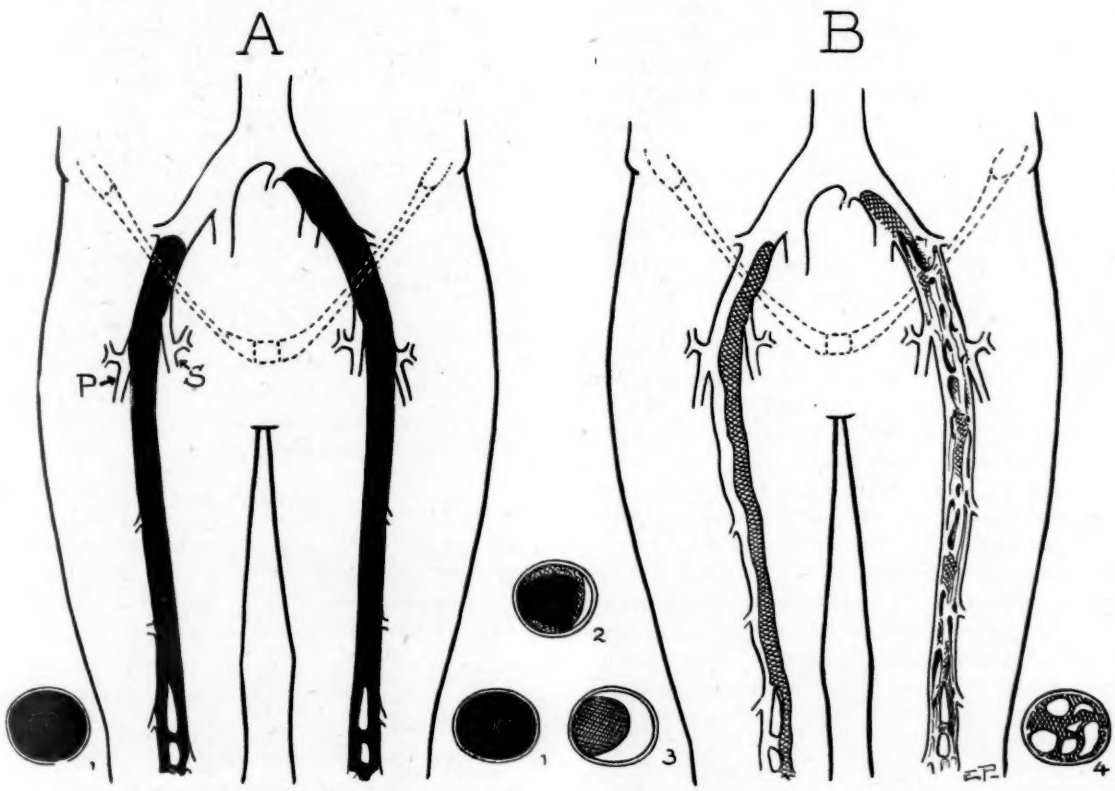

FIGURE 1. *Semidiagrammatic Scheme of a Bilateral Obstructive Thrombophlebitis in the Lower Limbs.*

The process extends higher on the left than on the right. A *represents the acute stage, before organization,* 1 *and* 1 *being cross sections of the thrombosed femoral veins.* B *represents a later stage. In the right leg, the thrombus has become a solid fibrous mass, shown in cross sections* 2 *and* 3. *In the left leg, the thrombus has been divided by multiple channels, shown in cross section* 4. *Both these conditions have been encountered on exploration.*

work of the functionless veins. Presumably, the great veins sometimes seen in the groin and upon the abdomen of those who have suffered a long-continued plugging of the femoral and iliac veins are, in the acute stage of obstruction, the principal means of transmitting the venous return from the legs. Later, as alternative routes, by means of valved veins within the muscular envelope, are opened up, these overdistended veins become functionally useless. One can easily demonstrate the downflow of blood in all such vessels by the tests applicable to varicose veins in general.

The once thrombosed femoral vein itself must also be presumed to be a direct source of congestion and leg may be studied and, if necessary, explored by a liberal incision in the groin. The saphenous vein should first be exposed and, if found diseased, divided at its point of entry into the common femoral. The femoral vein should then be inspected from this point downward for several centimeters — well below the entrance of the profunda femoris. It will usually be surrounded by scar tissue and will be

*Bauer's study of the sequels of thrombosis takes up, most thoroughly, many aspects of the problem but gives no descriptions of the actual state of the once thrombosed veins, as seen on section at the operating table or at autopsy. Moreover, his phlebographic evidence that the veins superficial to the muscular envelope constitute the principal collateral pathways, ignoring the great intermuscular plexuses and their deep connections with the pelvis, is decidedly open to adverse criticism. Perhaps the superficial veins do offer the easiest way out for the venous blood when the patient lies flat, as during phlebography, but this does not mean that deeper vessels are not used in the erect position and during exercise.

whitish, instead of its usual blue color. Often the heavy scar of the organized thrombus can be felt, the vein being a solid-feeling cord, which, however, is actually distensible. In the figure, the state of the femoral and iliac veins, as I have seen them on section at the operating table, is diagrammatically pictured. Whether I am right in believing that the canalizing process is as complete as I have suggested may, of course, be questioned. In any case, the vein that I have described is functionally useless and can be divided with impunity.

Far from aggravating the signs of venous stasis, a common femoral or iliac division results in lessened distention of the superficial veins and an improved color of the foot. Any edema that is present may be diminished, although edema and its complications are less likely than venous congestion to be relieved, as Coller and his associates[9, 10] have reported in studying the results of femoral-vein interruption. Their indications are mainly chronic induration and ulceration, rather than the venous stasis that I have described here, and the recurrent thrombosis described under Group 5.

If distended veins on the pubis and abdominal wall are proved to be functionless, they may be reduced in number and size by section and perhaps injection, but although my experience indicates that their obliteration does no harm, it has also shown that it is even more difficult to make permanent than is the case with varicosities of the legs.

Group 5. Cases of recurrent thrombosis, with or without embolism, naturally present no consistently abnormal appearances. The affected leg usually shows some of the aftereffects of the original thrombophlebitis. Pulmonary infarcts rarely recur without other evidence of old or fresh thrombosis, in which event it must be supposed that a thrombus forming in a canalized, useless vein is locally silent. I have a record of one such case, in which repeated pulmonary infarction simulated angina pectoris and the patient had been made an invalid.[11] Section of the external iliac vein prevented further recurrence. On division of the vein, ribbonlike masses of scar tissue were noted, much like those shown in the figure.

In other cases, there has been a history of recurrent swelling and lameness of the calf. In yet others, small superficial local thromboses have pointed very strongly to the presence of a deeper process, of which they are merely a complication.

Although section of the common femoral vein must often serve, the ideal treatment for all such recurrent thromboses is ligation of the corresponding common iliac vein, because this high division secures the best collateral venous circulation and gives the greatest help in the prevention of future thrombosis and embolism. Unfortunately, a previously, and perhaps repeatedly, thrombosed common iliac vein is difficult and sometimes dangerous to deal with, for it is frequently found to be both adherent and fragile, requiring the greatest care in handling. Ligation of the vena cava may even be required.

Summary

On the reasonable presumption that femoroiliac thrombophlebitis is the usual end stage of thrombosis in the deep veins of the leg, an attempt has been made to group the various abnormal states that follow such a thrombophlebitis. Five groups of patients have become distinguishable among the ambulatory persons who present themselves as office patients — namely, those characterized, respectively, by edema, by edema plus induration, pigmentation and ulceration, by a pain complex, by venous congestion and by recurrent thrombosis.

These groups overlap, yet by a study of the clinical history and physical signs, every patient can be placed, for purposes of treatment, in one group or another.

Appropriate means of treating the members of each group are suggested.

It will be a matter of great interest to discover how modern treatment, especially of the earlier stages of venous thrombosis in the lower limbs, — that is, by operation and anticoagulants, — influences the establishment of femoroiliac thrombophlebitis and its late results.

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Discussion

Dr. E. Everett O'Neil (Boston): This is a new grouping of cases that Dr. Homans has outlined, and for anyone who sees a large number of these conditions, it is an excellent working formula. The second group that he mentioned, which manifests itself by a tremendous amount of induration and ulceration and scarring in the lower inner third of the leg, represents what is probably one of the most difficult venous conditions with which the surgeon has to deal. This problem has engaged my interest for several years.

The third group mentioned, in which pain alone is an outstanding phenomenon, has not in my experience been observed alone. It is usually found, so far as I am concerned, in conjunction with the other phenomena of ulceration, induration and scarring.

So far as the treatment of the second group is concerned, — and to me this is the most important of the five groups, — I

am going to go farther than Dr. Homans and tell you what my experience has been in treating these cases. Long ago I was disturbed by seeing so many cases of obviously deep thrombophlebitis, characterized by thrombophlebitic ulcers without varicose veins, and with a history of repeated high saphenous divisions, without any obvious improvement in the ulceration.

As long ago as twenty-five years, Dr. Homans suggested that the flap operation in the lower leg, with division of the perforating veins, might well be the answer. Dr. Linton, I think, revived this idea, and suggested that these flap operations be more extensive, that they be done also in the lateral aspect of the leg, and that the appropriate perforating veins be divided. This does not seem to me to be sufficient. In addition, Dr. Coller has suggested femoral divisions. This is not the answer.

Most of these cases, as Dr. Homans has suggested, are associated, with reflex arterial spasm, which manifests itself by increased sensitivity to cold, increased sudomotor activity and the typical brawny edema and stiffness of the extremities, sometimes with atrophy of bone. I have come to believe that, after these patients have been subjected to procaine block, if they seem to improve, they should be immediately subjected to sympathectomy.

There is no doubt in my mind that patients who have had chronic thrombophlebitis have a tendency to develop recurrent thrombosis. If this is so, there is a grave danger of their developing a propagating thrombus and a lethal embolus. Heretofore my routine procedure has been to do a primary division of the superficial femoral vein, followed by lumbar sympathectomy. I have found that this is not enough, and have dissected the lower leg as well, doing a flap operation. Only by this method, I am sure, can one begin to salvage some of these unfortunate cases.

This seems like a great deal of surgery, but, as Dr. Homans has mentioned, it makes little difference how much one divides these deep vessels so long as one does so high enough and performs the subsequent operative procedures that clear up the lesions.

Concerning injections in postphlebitic legs, I mention them only to condemn them, because they are of no value and should not be done. This procedure is in the same category as dividing saphenous veins for deep thrombophlebitis.

DR. HOMANS (closing): I should like to say a word more about the pain complex, which fascinates me. Actually one does see it without other signs, in a leg that may look almost normal or show only a little bit of edema. Yet the patient makes a bitter complaint on having to stand a good deal and on taking exercise.

The most obvious things that one finds in going over a patient suffering from a pain complex are the peculiar, stocking-like paresthesia, which makes one think it is a hysterical affair, and the tenderness or soreness felt on compressing on the calf. These are the signs that mark this condition and the signs that are relieved, along with the pain, by blocking the sympathetic system. I have not paid so much attention as I ought to, perhaps, to the pain problem in the presence of other postphlebitic difficulties.

There is one matter that should not be slighted in treating these postphlebitic states, and that is the varicose veins that actually may develop, probably because of the dilatation that takes place while the main venous pathway is obstructed. One has to deal with these as one would deal with any varicose veins. It is well to have this in mind, but do not operate on a saphenous vein thinking you are going to cure the postphlebitic lesion. You may help it a little when the vein is obviously varicose, but the old idea of excising great areas of scarred and ulcerated tissue I have given up, probably because of increasing years. It is hard work and one does not get so much result from one's effort as one would like. Instead, a great deal can be accomplished by lessening the edema and treating the skin in the postphlebitic states, and thereby one is spared, and the patient is also, the labor and difficulty of some of these elaborate procedures.

DEXTROCARDIA AND BRONCHIECTASIS

A Review of the Literature and a Report of Two Cases

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IN THIS decade of increasing mass radiography, when the United States Public Health Service, state health departments, tuberculosis associations, private industries and other agencies are interesting themselves in x-ray survey programs, it is not amiss to call attention repeatedly to nontuberculous diseases of the chest. In most cases during the conduct of chest x-ray surveys, persons who are found to have such abnormalities are referred to their private physicians — not to specialists — for further investigation. Consequently, it is incumbent on progressive physicians to become well versed in the roentgenographic as well as the other aspects of diseases of the chest. Although no disease of the chest constitutes a public-health problem of the magnitude of pulmonary tuberculosis, others are of paramount importance to the health, welfare and livelihood of those persons concerned.

The purposes of this paper are to report 2 cases of dextrocardia and bronchiectasis, to call attention to this clinical entity among nontuberculous diseases of the chest, which will be recognized more frequently during the ensuing years and to present evidence that transposition of the viscera is attended by a high incidence of other significant abnormalities.

The coincidence of bronchiectasis and dextrocardia was first reported by Siewert[1] in 1904. From that time until 1933, only 2 additional cases appeared in the literature.[2, 3] At that time, in recording 4 cases, Kartagener[4] observed the coincidence of sinus disease in association with bronchiectasis and visceral transposition. The simultaneous occurrence of these three conditions has been termed "Kartagener's triad." Kartagener, who was a proponent of the theory of the congenital origin of bronchiectasis, maintained that these cases lent proof to this tenet. In 1935, Kartagener and Horlacher[5, 6] reported 7 additional cases, which were found in several European clinics.

Two years later, Adams and Churchill[7] published the first paper in the English language on this subject. Among 23 cases of situs inversus, they found 5 with bronchiectasis. A review of embryologic data

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led them to conclude that the bronchiectasis in these cases represented a stigma of maldevelopment. In 1943, Olsen[8] reported 14 cases of bronchiectasis among 85 patients with dextrocardia. This is the largest single group of cases reported to date.

Besides the reports already mentioned, the following are noted: Nüssel and Helbach's[9] 2 cases and single case reports by Behrmann,[10] Casaubon and Derqui,[11] Wernli-Haessig,[12] Glaum,[13] Becker,[14] Rosenthal,[15] Ingraham,[16] Cole and Nalls,[17] Nagy,[18] Adland and Einstein,[19] Meyer,[20] Richards[21] and Delp.[22] Including the 2 cases that follow, there are 50 cases of dextrocardia and bronchiectasis on record.

Case Reports

Case 1.* L. M. O., a 34-year-old man, was admitted to the Bryce Hospital, Tuscaloosa, Alabama, in 1934 with a diagnosis of mental deficiency and psychosis. In the past he had been subject to frequent respiratory infections and severe sore throat. The family history was noncontributory.

On examination the patient was found to be dull and childish. He coughed frequently, producing foul, yellow, tenacious sputum. The significant findings were as follows: a deviated septum with both nares occluded by a mucopurulent discharge; dental caries and fetor oris; diffuse injection of the pharyngeal mucous membrane with copious postnasal drip; palpably enlarged lymph nodes in the anterior cervical chain; dextrocardia with no enlargement, arrhythmia or auscultatory abnormality; an admixture of dry and moist rales over both lower lung fields; and evidence of transposition of the abdominal viscera.

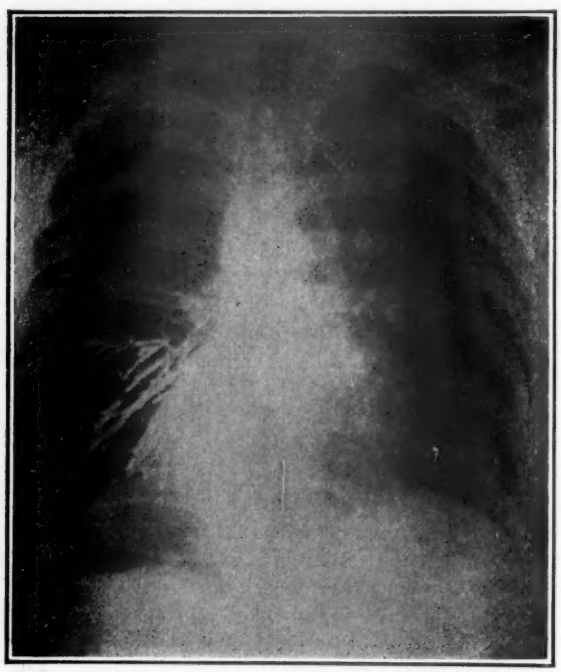

Figure 1. *Case 1.*

Additional studies included a conventional radiogram of the chest, which demonstrated the dextrocardia. The bronchial markings into both lower lung fields were decidedly exaggerated, and there was evidence of peribronchial inflammatory change. Bronchography of the right lower lobe (Fig. 1) showed a cylindrical type of bronchiectasis. A plate of the sinuses demonstrated a bilateral chronic frontal and maxillary sinusitis.

*This case is reported with the permission of Dr. W. D. Partlow, superintendent of the Bryce Hospital. It was correctly diagnosed on 35-mm. film, being discovered during the conduct of a survey for tuberculosis.

Case 2. P. S., a 7-year-old girl, is the private patient of one of us (H. W. K.). The prenatal history and delivery were uneventful. Within 24 hours after birth the infant had cough and cyanosis. X-ray examination of the chest at that time revealed dextrocardia, without parenchymal change. There was subsidence of the cough and cyanosis within a few days. The patient had had a chronic cough productive of a mucoid expectoration since early life. When 4 years of age, she received tonsillectomy and adenoidectomy. Following this procedure, it is believed that the cough became less productive. At 5 years of age, the patient had an uncomplicated case of chicken pox. For years the patient had had frequent upper respiratory infections, associated with rhinorrhea and postnasal discharge. During the year previous to examination, a diagnosis of sinusitis was made by an ear, nose and throat consultant.

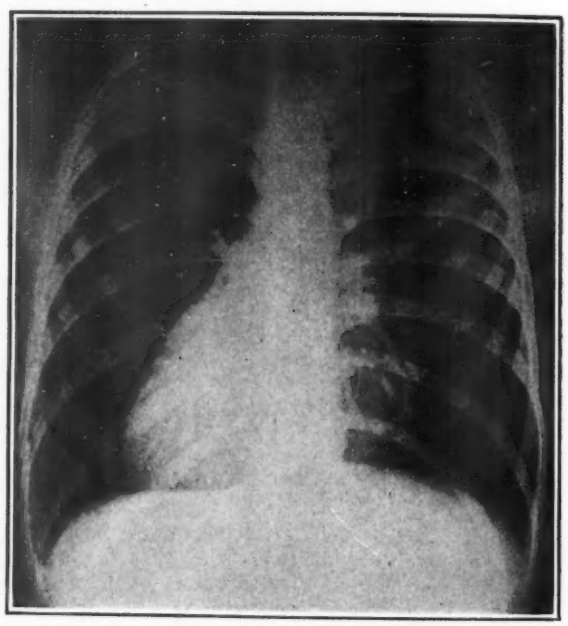

Figure 2. *Case 2.*

On physical examination, the patient was found to be well developed. There was no evidence of cardiorespiratory distress, although there were a frequent moist cough and questionable cyanosis. Significant physical findings were dextrocardia, with no enlargement, arrhythmia or murmurs, moist and dry rales over both lower lung fields posteriorly and transposition of the abdominal viscera.

A conventional posteroanterior radiogram of the chest showed the dextrocardia to be associated with a generalized increase in the bronchial markings. On the left side, the cardiohepatic angle was obtunded by soft flocculent shadows. In the right lower lung field, there was evidence of peribronchial inflammatory change.

Lipiodol was instilled into the right lower lung field by Dr. Robert M. Lowman, radiologist of the Grace Hospital, New Haven, Connecticut. Under fluoroscopy a cylindrical dilatation of the second and third dorsal bronchi could be visualized (Fig. 2).

One of the valuable byproducts of mass radiography in the control of tuberculosis is the detection of nontuberculous pulmonary disease. Gould[23]

found that 1.13 per cent of 442,252 persons examined in surveys showed some type of significant nontuberculous aberration. Of the entire group, 0.6 per cent had abnormal hearts, whereas 0.009 per cent (approximately 1 in 11,000 persons examined) had dextrocardia. Scatchard and Duszynski[24] reported 1 case of dextrocardia in 2721 roentgenographic examinations in a general hospital. Morse[25] found 36 cases among 223,182 examinations, a frequency of 1 in 6200. Russakoff[26] has observed 6 cases among 36,717 persons examined in surveys, a frequency of 1 in 6120.

Olsen[8] in reviewing the files of the Mayo Clinic from 1920 through 1941 found 85 cases of dextrocardia. Of these, 14 were discovered to have an associated bronchiectasis, an incidence of 16 per cent. During this identical period a diagnosis of bronchiectasis was made on less than 0.5 per cent of all other patients investigated. Thus, the frequency of bronchiectasis in this series was thirty-three times as great among persons with dextrocardia as among a representative clinic population. Kartagener and Horlacher[5] found 23 per cent of their patients with dextrocardia to have bronchiectasis, and Adams and Churchill[7] found this correlation to exist in 22 per cent of their group. It is interesting to note that Morse[25] reported 1 case of bronchiectasis in his group. His study, however, deals only secondarily with cases of dextrocardia, and it is therefore assumed that a complete study for bronchiectasis in all cases was not made.

Although it may justifiably be argued that the true incidence of bronchiectasis in a representative clinic population is probably in excess of 0.5 per cent, it is still undeniable that the coincidence of bronchiectasis with visceral transposition is unusually high. Thus, the obvious conclusion to be drawn from these studies is that the consistently high incidence of bronchiectasis among patients with dextrocardia is hardly to be explained as a chance occurrence.

Dextrocardia is altogether too frequently considered to be an anomaly of little if any significance; yet Olsen[8] observed that 11 of his patients, exclusive of those with bronchiectasis, had additional significant defects and 2 others had cardiospasm. Thus, of 85 persons with dextrocardia, 32 per cent had other significant abnormalities.

* * *

These observations obligate physicians to adopt a somewhat different attitude toward cases of dextrocardia. It is no longer sufficient to inform the patient of transposition of the abdominal viscera in cases of situs inversus to avert the catostrophes of improperly interpreted contralateral abdominal manifestations. Besides a search for other anomalies, a thorough investigation of the upper respiratory system and the bronchopulmonary tree should be an integral part of a complete clinical study. Bronchography should perhaps be performed with less conservatism in such cases than is practiced among patients without dextrocardia.

With recognition of the fact that more cases of dextrocardia are bound to be uncovered in practically every community as a byproduct of mass radiography in the control of tuberculosis, it is timely that physicians take cognizance of the high incidence of significant abnormalities associated with this condition.

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MEDICAL PROGRESS

ACTIVE IMMUNIZATION

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THE continued extension of public-health and preventive medical activities, the need for new and massive immunization programs among the armed forces of the United States and other countries, and the corresponding impetus that the war gave to investigations concerning active immunization have in recent years produced an enormous mass of theoretical and experimental observations in this field.

In this review no attempt is made to cover any branch except active immunization as it applies to diseases existing in New England for which such immunization is of practical interest — that is, diphtheria, scarlet fever, tetanus, pertussis, typhoid fever, smallpox, influenza and rabies. Even within this range, the review is essentially incomplete, in so far as it omits many subjects that are now primarily of theoretical interest but on which important future trends in active immunization may depend. Such topics as the mechanisms of immunization, the immediate and late effects of hypersensitization and their underlying mechanisms, the so-called "interference phenomena" that have recently come to light — especially in the field of virus infections — and the significance of nonspecific protein reactions (among which may be included the recently publicized antireticular cytotoxic serum of Bogomolets[1]) are inseparably related to active immunization but, for practical reasons, cannot be considered.

All the commercial laboratories and several of the larger state and municipal laboratories preparing biologic products for immunization operate under licenses from the Federal Security Administration, through the National Institute of Health of the United States Public Health Service. Such laboratories, which are regularly inspected by officers of the National Institute of Health, must, with few exceptions, submit samples and protocols of each batch of the product distributed, must clearly label the package in certain specified respects and must conform to certain minimum requirements governing safety and, generally, potency. Consequently, one may be reasonably certain that such products are not harmful, and that, so far as practicable, their effectiveness is maintained above a specified minimum. Beyond these limits, however, the National Institute of Health recognizes that large areas exist within which possible improvements in methods of production, testing and use may be found. Concurrently, continuing studies of all types of research, as well as extensive applications of biologic products to human patients by clinicians and public-health workers, guarantee that no product or method will remain static for long. Moreover, since epidemic disease knows no artificial boundaries, the advances in this field have been world wide; the material presented below has accordingly been drawn from almost as wide a range as the scope of the diseases in question.

Several general textbooks and reference books published in recent years have given considerable space to the preparation or the use of biologic products.[2–6] Such texts are of great value for general information and reference. Each includes primarily topics of particular relevance to the text, and therefore each must be supplemented with data from other sources, to cover wider areas as well as to bring the information contained up to date. Current advances in the related subject of diagnostic skin tests have recently been reviewed.[7]

DIPHTHERIA

The decline in the diphtheria case and death rates, which began many years ago, has been greatly accelerated by the use of artificial immunization, so that within the last few years case rates of less than one hundredth of those sixty years earlier have been recorded, as in Massachusetts.[8] This decrease has been accompanied by a tremendous decline in the carrier rates in artificially immunized communities, and hence in the frequency of naturally acquired stimuli to immunity, in turn apparently related to a widely noted decrease in the general level of immunity in certain sections of the population. Schick-test surveys among young adults or adolescents in England, Canada, Australia and the United States have shown that 50 to 60 per cent are susceptible to diphtheria,[9–16] in contrast to the incidence of 20 to 25 per cent of positive reactions formerly reported in these age groups.[17] Thus a growing reservoir of young adults susceptible to diphtheria appears to exist. A parallel consequence of the reduced prevalence of diphtheria bacilli is that artificially induced primary immunity is likely to wane and disappear more rapidly than

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formerly. Hence present control of diphtheria must be concerned not only with immunization of a wider age group than previously but also with the necessity of maintaining immunity once it has been established. In the application of procedures under these circumstances, several points deserve particular consideration.

Choice of immunizing agent. The antigenic superiority of toxoid over toxin-antitoxin has long been established.[18–20] When the slight though real dangers of serum sickness from toxin-antitoxin[21] and the inherent risk of administering a toxic preparation[22] are also considered, there appears little justification for its continued use except under special circumstances. The principal choice thus narrows down to FT (fluid toxoid) versus APT (alum-precipitated toxoid). Both, when properly used, are extremely effective as judged by the production of a negative Schick test. Fraser and Halpern[23, 24] and Volk and Bunney[25] found that about 95 per cent Schick reversals may be observed a few months after administration of two doses of APT or three doses of FT. It is possible that APT is slightly superior to FT, but the difference is considerably less than can be observed, for example, between good and poor batches of APT.[9, 26, 27] The experience of recent years suggests that occasional or perhaps periodic reinforcing doses of toxoid are required to replace the stimulus no longer provided by the diphtheria carrier. Such repeated doses increase the possibility of allergic reactions to constituents of the toxoid, and it has been variously demonstrated[28–30] that alum precipitation markedly enhances the capacity of toxoid and other antigens to produce reactions of hypersensitiveness. Thus, Fraser[24] warns against the possibility of obtaining undesirable anaphylactic reactions when immunity is reinforced by a subsequent dose; since APT is extremely effective in rendering guinea pigs sensitive and anaphylactic, the administration of a second or subsequent dose at long and irregular intervals may increase the danger of such reactions in man. Additional objections raised against APT are the greater frequency of local reactions,[31–33] the localization of smallpox vaccination at a site recently injected with APT[31] and the difficulty of maintaining a uniform suspension, particularly in mass immunization.[34] It should be noted, however, that allergic reactions to APT are extremely rare and that studies suggest that similar reactions to tetanus toxoid can largely be ascribed to the presence of an obsolete ingredient in the medium rather than to the bacterial protein itself.[35] Moreover, APT has the definite advantage of requiring only two instead of three doses for adequate primary immunization. This may therefore prove to be the agent of choice wherever geographic, educational or administrative factors make it difficult to ensure completion of three doses, whereas FT may be preferred wherever the completion of a three-dose schedule presents no major problem. With either agent, it should be possible to obtain a toxoid free of antigenic constituents other than those caused by the diphtheria bacillus itself, since Mueller et al.[36–38] and others[39–41] have demonstrated that a potent FT or APT can be produced on a peptone-free medium. Such a medium has been used for the entire production at the Massachusetts Antitoxin and Vaccine Laboratory for over six years.

Preferred dosage and interval. There is no longer any justification for attempting immunization with one dose of APT or two doses of FT except in an emergency, although these inferior methods give better results than no immunization.[42, 43] Both systems have had their vogue, and both are now generally discredited as being insufficient to produce an adequate, sustained immunity,[24, 25, 43, 44] although Bousfield[45, 46] and others maintain that, when diphtheria is prevalent, adequate results may be obtained with one dose of APT. The recent description of a diphtheria outbreak among a group of children, most of whom had received one dose of APT,[47] and similar experiences[48] testify that such a procedure does not protect effectively against intimate exposure to virulent bacilli. Proper immunization, therefore, is still based on two doses of APT or three of FT. Likewise, proper immunization depends on spacing the doses at least three weeks apart, regardless of which agent is used. The practice of giving successive doses of APT one week apart seems never to have arisen, but it is still widely supposed that an interval of a week is sufficient when FT is used, despite Ramon's[49] evidence to the contrary many years ago. Numerous recent studies have shown that a longer interval is also advantageous when APT is used.[50–52] Furthermore, experience with tetanus toxoid, pertussis vaccine, typhoid vaccine and other immunizing agents points to the advantages gained by lengthened intervals between doses.

Various British studies on APT immunization have recently reopened the question of the optimal size of dose.[9, 26, 27, 45, 53] The evidence suggests that doses as small as 0.1 to 0.3 cc. are effective.[9] These studies were for the most part carried out in areas where diphtheria was more prevalent than in the United States; also the subjects were not followed up with Schick tests later than four or five months after immunization. The results must therefore be re-evaluated before they can be judged in the light of American conditions and standards.

Results obtained with toxoid. As suggested above, the results obtained vary with many factors, among the most important of which is the interval between immunization and follow-up. Fraser and Halpern[54] have shown that three months after immunization with three doses of FT, a large number of previously susceptible children had over 0.02 unit of antitoxin per cubic centimeter of serum; this is more than five times the amount necessary for the production

of a negative Schick test,[55] which in turn is generally correlated with resistance to diphtheria.[7] A year later 3 per cent and three years later 8 per cent of the group were Schick positive; whereas five years later 34 per cent had reverted to the Schick-positive state, and the average serum antitoxin titer was only 20 per cent of the maximum obtained shortly after immunization.[56] A more recent study indicates that among young adults the relapse rate may be as high as 20 per cent in one year.[57] Thus, the protection against diphtheria observed in any large group decreases in proportion to the interval since inoculation. Nevertheless, the clinical protection afforded by toxoid immunization is impressive. With few exceptions[58, 59] the incidence of diphtheria among immunized persons averages about 10 to 15 per cent that among nonimmunized controls.[43, 60–62] Moreover, diphtheria is usually milder in inoculated than in unimmunized persons.[62–65] Occasional cases occurring in previously immunized patients, however, sometimes arouse doubts concerning the efficacy of immunization in general; it is only by adjustment of the observed case rates to the relative numbers of the immunized and unimmunized persons, as Gibbons[60] has done, that the high degree of protection actually achieved by immunization is made clear.

Immunization of adolescents and adults with toxoid. In virtually all the usual immunization programs, diphtheria toxoid is the only agent used. The provision of toxin-antitoxin mixture in Massachusetts for group immunization is being continued temporarily because of long familiarity with this agent — particularly for adult immunization — and the admitted difficulties arising from the relatively frequent reactions experienced by adolescents and adults receiving toxoid in the routine dosage. Extensive experience in Canada and several states in this country, however, indicates that reactions can largely be avoided by the inoculation only of persons who are Schick positive, the performance of the Moloney test, using 0.1 cc. of diluted toxoid, on the Schick positives[66–68] and the administration of divided doses of toxoid or diluted toxoid to subjects showing positive Moloney reactions.[69] The usual initial dose in older subjects is 0.1 cc.[70, 71] which has in fact on occasion been substituted for the Moloney test.[72, 73] Recent observations suggest that immunization should be withheld from persons exhibiting any reaction to the Schick control test,[16] which should therefore always be employed in subjects tested in these age groups, since such reactors almost always possess either actual[55] or latent[16] immunity and usually show marked reactions to toxoid.[74] Furthermore, Wishart et al.[75] and Paschlau[76] have noted a direct correlation between severity of reaction and degree of immunity, so that in group immunizations one may safely leave the toxoid reactors with a single stimulus from the Schick or Moloney test, or both. This principle has been followed on a large scale in military establishments.[72]

Other immunization routes. Numerous workers have experimented with intranasal immunization with toxoid by drops[77–80] or spray.[81] As a procedure for primary immunization, the intranasal route appears less potent than the parenteral, whereas its use for reimmunization is likely to lead to severe and peculiarly uncomfortable reactions in persons who have acquired a sensitivity to toxoid. Percutaneous immunization[82] has been tried without success, and intradermal immunization[83–86] has also been employed, with better results in some hands[85] than in others.[86] As might have been expected, reactions were more marked following intradermal administration of APT than when FT was used.[85, 86]

Bousfield,[87] who[88] has explored various unusual routes of immunization against diphtheria, has recently suggested the use of toxoid pastilles to be sucked like hard candy. He reports that evidence for their effectiveness in primary immunization is lacking, but that they elicit an effective booster response and do not provoke local or general reactions. Finally, mention should be made of the protamine-toxoid combination developed by Ross,[89, 90] which appears to be remarkably high in potency and which produces little reaction. Both preparations warrant further study.

Reimmunization. The importance of reimmunization at some time subsequent to the primary immunization is apparent from the findings cited above. The dose required is often exceedingly small. Twenty years ago Glenny[91] called attention to the booster effect frequently observed after a Schick test performed with material containing about one fifteen hundredth as much antigen as the corresponding volume of the average toxoid. Wishart et al.,[75] Volk et al.,[92] Wilkey[93] and others have presented impressive evidence of the rapid and powerful effect of a booster dose of toxoid in persons with previously acquired immunity. The rises observed may be tremendous (over seven thousand times the minimum protective titer) and long lasting (three months or more).[16] Nevertheless, adequate responses were not recorded in some subjects until about a week had elapsed,[75] so that the method is not completely dependable as an immediate protective measure following exposure to diphtheria. For the routine maintenance of group immunity, however, it has quite properly been widely advocated as a periodic health measure, particularly in localities where the natural incidence of diphtheria is too low to provide the necessary booster effect.[94]

Immunization of infants. It has long been taught[95] — and is doubtless generally true — that the best time for immunization of infants is after the first six months, because prior to this period the passively inherited maternal immunity interferes with the active effect of toxoid. Yet such a postponement leaves unprotected the currently increasing number

of infants whose mothers are not immune. Where diphtheria is prevalent, its occurrence in infants represents a real danger, for it can readily produce an atypical and overwhelming infection.[96] Liebling, Youmans and Schmitz[97] have offered a partial solution to this problem by antenatal immunization of Schick-positive mothers. A small group whose response was followed beyond the neonatal period, however, indicated that the immunity thus transferred to the infants was even shorter lived than the inherited natural immunity.[98]

Combined immunization with diphtheria toxoid and other agents is discussed below, under tetanus, pertussis and typhoid fever, since such combinations are usually designed to incorporate other agents into an established procedure for diphtheria immunization.

Scarlet Fever

The many factors involved in the medical and administrative control of scarlet fever have recently been thoroughly reviewed.[99] There is fairly general agreement that streptococcal toxin prepared, standardized and used according to the methods prescribed by the Dicks[100] prevents the development of clinical scarlet fever in a great majority of persons exposed. In this respect Anderson's[101] review of a decade ago is fully valid today. Place,[102] Lucchesi,[103] Toomey[104] and others have confirmed the numerous earlier reports that immunization according to the Dick method practically abolishes the occurrence of scarlet fever among nurses working in contagious wards. Graham[105] reports that follow-up Dick tests were negative in 86 per cent of 50 private patients tested five to ten years after immunization, and in 84 per cent of 30 subjects thirteen to fifteen years after inoculation. Little[106] observed 63 cases of scarlet fever among 6982 immunized subjects observed over a seven-year period, in contrast with 915 cases among 8063 unimmunized persons — an attack rate of 0.9 per cent in the former as against 11.3 per cent in the latter.

Such an effective procedure would have been universally accepted long ago if it did not have definite drawbacks. Foremost among these are the frequency and severity of the reactions produced by the dosage of the subcutaneous injections of toxin recommended by the Dicks, which are usually 650, 2500, 10,000, 30,000 and 100,000 to 120,000 STD (skin test doses) at weekly intervals. There is still, as Anderson stated,[101] surprising unanimity of opinion regarding the severity of reactions to toxin injections, most observers mentioning severe reactions in as many as 10 or 15 per cent of cases. Jacobs and Orris[107] report an incidence of 28 per cent of moderate or severe reactions, including nausea, vomiting, fever and a rash comparable to that of mild scarlet fever itself. Less frequent, but perhaps highly significant, is the occurrence of joint manifestations,[108] which have been found to exhibit a high degree of association with a history or signs of rheumatic fever. Such a relation possibly explains the reported fatal reaction occurring in a thirteen-year-old boy following an initial 500 STD of scarlatinal toxin.[109] At all events, it becomes difficult to justify the widespread use of a procedure that may cause reactions such as those described. Moreover, there is considerable doubt whether the scarlatinal rash is produced by only one antigenic type of toxin.[110] Hence, with the various factors concerned taken into consideration, it has been authoritatively stated that information is at present sufficiently convincing to render immunization against scarlet fever as a routine or community-wide practice under official auspices inadvisable until a more suitable antigen becomes available.[111]

Nevertheless, certain groups must be immunized, particularly physicians, nurses and ward attendants likely to come in contact with cases of scarlet fever. Also, the relatively high incidence of susceptibility among young adults, as evidenced by the Dick test or by clinical experience, can be of serious concern to military establishments and in civilian communities during high prevalence of the disease. Many attempts have therefore been made to overcome the difficulties encountered with the standard immunizing procedure by modifying the dose, the administration route or the antigen itself. Howie[112] employed a dosage schedule widely used in Canada (330, 1000, 2300, 5000 and 10,000 STD) in the immunization of over 8000 school children at the onset of an epidemic of scarlet fever in Windsor, Ontario; five months later, 89 per cent of a representative sample of the group were Dick negative, and statistical data indicated that the epidemic had been checked, in contrast to the neighboring city of Detroit, where it continued unabated. Glazier[113] immunized 340 children over a period of years with seven weekly doses of 650, 2500, 5000, 10,000, 25,000, 55,000 and 110,000 STD respectively; reactions occurred after only 7 per cent of the injections, and Dick tests (one week after the last dose) were negative in 265 out of 268 children tested. None of the 340 patients subsequently developed scarlet fever.

Others have tried intranasal, percutaneous, intracutaneous and oral administration of the toxin; Graham has reviewed most of these studies.[114] The intracutaneous route has given excellent early results in some hands,[115–118] although as many as ten doses were required in individual cases to produce a negative Dick test.[117] Late follow-up Dick tests, however, indicated that a large number of the patients had reverted to the Dick-positive state.[107, 117] As indicated elsewhere, there is increasing reason to believe that the intracutaneous route is probably not dependable for routine primary immunization, although it can doubtless be used successfully in carefully handled individual cases. Results with the percutaneous, intranasal and oral routes, including 59 of Graham's patients given toxin intranasally, in-

dicated on the average a lasting immunity of about 60 or 70 per cent, although better results may be found in early follow-up Dick tests. Several years ago the Dicks[119] reported that 93 per cent negative tests were obtained following the oral administration of over 8,000,000 STD in enteric-coated tablets. The wider development of this method has been hampered by the expense of preparing this quantity of toxin in powdered form and by the difficulty of ensuring its proper absorption. No recent reports on this interesting method have been noted.

Attempts have been made to reduce the reactions following scarlatinal toxin injection by purifying the crude toxin. Stock,[120] Veldee[121] and others have employed various methods for separating the toxin from the other constituents of the medium; it is in fact possible to prepare toxins of extremely high purity by such means. In these preparations relatively few side reactions are caused by impurities, but their primary toxicity is unchanged. Hence, other means of preparing a tolerable product must be resorted to. Several workers have prepared toxin precipitated with alum[122] or adsorbed on aluminum hydroxide.[123–125] Menten et al.,[125] who for unexplained reasons refer to their product as a "toxoid," found that it yielded a higher Dick-negative rate than that observed in other groups immunized with a fluid toxin, and that it caused fewer reactions. The possibilities of this procedure call for further study.

Veldee et al.[126] have prepared a tannic-acid-precipitated, purified toxin that, modified slightly, was used in an extensive field study, comprising over 41,000 person-years of observation in an immunized group and a carefully analyzed and much larger control group. It was demonstrated that approximately 87 per cent of Dick-positive reactions in children before immunization became negative and remained so for four years after immunization with three intradermal injections of 750, 3000 and 10,000 STD of this toxin at intervals of two weeks. Similarly, the incidence of scarlet fever among the entire immunized group was only about one fifth that in the control group. Reactions were rare, and no child or parent refused to complete the entire course. The study was carried out with very thorough and accurate statistical and epidemiologic controls. The results appear highly promising, and it is hoped that, since a tannic-acid-precipitated toxin has been approved by the Council on Pharmacy and Chemistry of the American Medical Association,[127] further trials of this preparation will be forthcoming.

Attempts to produce a scarlet-fever toxoid have been carried out by numerous workers. Following the encouraging results obtained by Veldee,[128] a formalinized toxin was given extensive trial in Massachusetts. A preliminary report by Anderson[129] on the results with such a preparation, administered in doses of 0.1, 0.5 and 1.0 cc. subcutaneously at intervals of three weeks, showed that approximately 52 per cent Dick reversals were obtained, and that the number of cases of scarlatina in the immunized group was only about 60 per cent of that to be expected from analysis of the control group. Reactions to the product were few and mild, and only 11 per cent of 9200 children failed to complete the course of three injections. Results obtained with subsequent and more potent batches of toxoid have probably been better than Anderson's figures indicate.[130] Unless strikingly improved immunization can be produced with such a preparation, however, it will probably be abandoned in favor of one with a higher antigenic potency. Since the Scarlet Fever Committee patent expired four years ago and since the restrictions on the free development of scarlet-fever prophylactics other than the Dicks' immunizing toxin have accordingly been removed, it can be expected that active and productive research in this heretofore relatively static field will proceed vigorously to the development of a satisfactory prophylactic agent.

Tetanus

Tetanus has always been a serious menace to war casualties, but even under the conditions of Western civilization in peacetime the possibility of its occurrence must constantly be borne in mind. Adequate cleaning and débridement of wounds remains the first defense against tetanus. Treatment of wounds can never be relied on to prevent all cases, however, for as many as 50 per cent may not be traceable to a known injury[131, 132] and many other cases follow neglect of such minor infections as those produced by a splinter. Since the tetanus bacillus is found even in city streets,[133] the possibility of infection with this organism is ever present.

Until recent years protection against tetanus was obtained largely through the prophylactic use of tetanus antitoxin. MacConkey[134] reviewed the experience with this agent in World War I and called attention to the occasional failures to obtain protection. Failures are also recognized in civilian experience; of the 146 tetanus cases reported by Dietrich,[131] Klopp[135] and Kirtley,[136] 11 patients had received prophylactic antitoxin, and 8 of the 11 died. Among a group of 15,000 to 20,000 casualties of the blitz of 1940 in England, 7 definite cases of tetanus occurred, in all but 1 of which 1000 to 1500 American units of antitoxin had been administered shortly after injury.[137] In the retreat from Dunkirk, 8 cases occurred in wounded soldiers who had never received toxoid and who had to rely on antitoxin prophylaxis.[138] Such irregularities appear to result mostly from the varied rate at which the antitoxin is eliminated from the blood stream.[44, 139–141] Thus the results obtained with prophylactic antitoxin are undependable, the more so because tetanus infection may exhibit a prolonged time lag between its introduction and its activation. Moreover, the disadvantages of antitoxin for prophylaxis are not limited to its undependability, as Bigler and Werner[44] have pointed

out. The wound may be so slight that medical aid is not sought or injury is not suspected. Antitoxin may not be readily available, the child may be allergic or may have received serum previously, and the ever-frequent serum sickness is always possible. Such considerations may influence the decision to take a chance and withhold serum.

The introduction of tetanus toxoid as an active immunizing agent offered a means of prevention that obviated many of these objections. The development and use of tetanus toxoid have been reviewed by Jordan and Halperin,[142] Newhouser[143] and others. A great many investigators have clearly established the capacity of tetanus toxoid to produce significant and presumably protective serum antitoxin levels in human beings. So many individual variables — such as age of patient, kind of immunizing agent, size of dose, interval between doses and accuracy of titrations — have been introduced that evaluation of the data in such studies is extremely difficult. Furthermore, the problem of interpreting the reported results is illustrated by such passages as the following:

> From the data it was deduced that when the initial tests were done within two months of giving the combined toxoids and the comparative tests showed the antitoxin values to be higher, the same or even lower after the respective third and second doses, then the tests performed from seven to twelve months later revealed not only that the drop of the titre was retarded after the third dose but that the antitoxin values were also higher.[144]

It is possible, however, within certain limits, to define the principal results by means of the following considerations.

Number of doses required. One dose produces almost no detectable immunity but prepares the subject to react effectively to subsequent doses.[145] Acceptable results are obtained by the administration of three doses of FT (fluid toxoid) or two doses of APT (alum-precipitated toxoid). Ramon[146] has from the beginning recommended three doses of fluid toxoid, and the inadequacy of two doses of this agent has recently been confirmed.[147]

Choice of interval between doses. For satisfactory results successive doses at least two weeks apart,[146] and preferably four weeks apart, are necessary. Peshkin,[148] Gold[149] and others have shown that excellent results are achieved even with intervals as long as two years between doses of APT. The limit to such extended intervals appears to be determined only by the period during which one can afford to wait before obtaining adequate immunity.

Choice of product. The principal advantages and disadvantages of each form of tetanus toxoid are essentially the same as those pointed out above for diphtheria toxoid. Dose for dose, APT is more effective than FT,[150–152] although the data in some cases are not properly comparable. The use of APT by the United States Navy and FT by the United States Army during the war should provide an unparalleled basis for comparison between the two, if the available data are ever analyzed.

Response to primary immunization. Practically all workers have observed marked variation in individual responses to primary immunization and have found occasional subjects in whom no detectable response appeared. In general, however, as with all immunization procedures for which accurate data are available, the antibody titer following primary immunization rises slowly to a maximum and then falls, at first rapidly and later more slowly, for as long as it can be detected. Obviously, the interpretation of results depends considerably on the interval chosen for the test. The actual interval between completion of immunization and development of a presumably protective antitoxin titer has been variously observed[35, 144, 148, 153, 154]; significant levels have been noted, however, as early as two weeks after immunization.

Protective level of antitoxin. Various workers have attempted — by analogy with titers observed following passive immunization[139–141] or by observing the titers in guinea pigs that were associated with protection against tetanus toxin[155, 156] or spores[157–162] — to estimate the level of antitoxin that will protect against clinical tetanus. These and other estimates range generally from 0.01[148, 155, 157] to 0.1 unit,[140, 159] but are of little practical value until they can be correlated with clinical experience, which has yet to be done.

Clinical evaluation. Massive clinical experience, although not correlated with serum antitoxin levels, has provided extensive statistical material for evaluating the efficacy of toxoid. Immunization of 40,000 horses in the French Army reduced the tetanus deaths in this group from the previous level of 50 to a single death.[163] In the retreat from Dunkirk, no cases of tetanus occurred among British soldiers protected with toxoid.[138] Among the more than 10,000,000 soldiers in the United States Army during World War II, there were only 3 known cases of tetanus in soldiers whose immunization record showed that the full immunization schedule had been completed.[164] The somewhat less perfect record in the British Army[165] may reasonably be ascribed to its policy of omitting the booster dose after injury and recommending antitoxin instead. Boyd[165] minimizes the value of the booster dose, arguing that it cannot be effective in less than ten days and that the infection itself serves as a booster after this interval in persons who have received primary immunization. It has been shown in animals,[161, 162] however, and in man,[144, 153, 154] that a marked response to toxoid appears by the fifth to seventh day. Moreover, this response is earlier and more effective in animals than the booster effect of infection itself.[161, 162] Boyd lists 22 cases of tetanus (with 11 deaths) among soldiers or others who had been protected with two or more doses of toxoid. Out of 15 soldiers in the British, Indian or Dominion

forces, 10 had received three or more doses. Only 4 men had been given four, and 2 had been given five doses. Since the standard procedure in the United States Army calls for at least four and usually five doses of toxoid as well as the emergency booster dose at the time of injury, the cases of tetanus reported here and elsewhere[166–168] in British and Colonial troops do not, as has been suggested,[169, 170] provide a valid criterion of the efficacy of tetanus toxoid prophylaxis performed according to current American practice.

The booster dose. On receiving a booster dose of toxoid, a previously immunized person exhibits a marked and rapid rise in serum antitoxin titer.[142, 144, 146, 150, 152, 171–173] Hence it has been generally advocated in this country that recall doses be given periodically, to restore the immunity level, which gradually falls after primary or later stimuli, and after injury to produce a maximal antitoxin level at the time of the greatest danger of toxin absorption. Some writers have assumed that the absorption of tetanus toxin in itself provides a sufficient booster effect,[150] but the available evidence indicates that tetanus infection does not act as a primary stimulus to antitoxin production[152, 159] and gives a secondary stimulus too late to be dependable.[161, 162] Therefore, until it is possible to define what constitutes a protective serum antitoxin level and to perform a simple test for the presence of this degree of protection, the only way to assure the maximum degree of protection is to make the most of the booster dose, by giving supplementary injections of toxoid following known injuries and by giving periodic doses to ward off the tetanus infections that can occur after unnoticed injuries. The efficacy of the booster dose does not appear to decrease as the interval between it and the primary immunization increases. Peshkin has obtained excellent booster responses one,[144] two,[174] three[175] and four[176] years after primary immunization. Furthermore, with each subsequent recall dose, the antitoxin titer usually rises higher and remains elevated longer.[175, 177] Yeazell and Deamer[141] employed intradermal toxoid successfully for the booster dose. It has been shown in animals that the booster response is but little affected by cold, restricted diet or overwhelming infection.[178] The only limiting factor in utilizing the booster effect appears to be the time interval between injection and response. The occasional subject whose response is slow might conceivably cause some anxiety, but clinical experience, as in the United States Army, strongly indicates that the rate of response to a booster dose is adequate. Finally, since the titer achieved following a booster dose remains elevated for several months,[144, 154, 174–176] frequent repetition of doses, such as those that must be relied on in prolonged antitoxin prophylaxis, is not necessary.

Other routes than the subcutaneous for administration of tetanus toxoid have been employed relatively little. Gold[179] and Sordelli et al.[298] gave booster doses intranasally, with apparently satisfactory results. Friedman and his associates[180] employed intradermal inoculations, but the results were decidedly less satisfactory than those obtained by the usual subcutaneous route.

Active-passive immunization. No clear-cut answer has yet been given to the dispute regarding combined active and passive immunization. In a patient exposed to tetanus, never previously immunized and requiring prophylactic antitoxin, one school of thought maintains that simultaneous commencement of active immunization with toxoid is ineffective because of the presence of excess antitoxin.[181] Another school has for over twenty years maintained that simultaneous active-passive immunization can be successfully practiced.[182, 183] The official policy of the United States Army has been to administer antitoxin prophylaxis only if an initial course of active immunization has not been completed and to start simultaneous active immunization.[35]

Allergic reactions. Such reactions, which have been reported to both FT and APT,[35, 151] have been amply reviewed by Long,[35] who showed that the urticarial type resulted from the presence of Witte or Berna peptone in the toxoid medium. The elimination of these ingredients from subsequent preparations has apparently virtually eliminated this type of untoward reaction. One of Swartz's[184] cases, however, may have represented a sensitivity to some ingredient in the toxoid other than peptone. The studies of Mueller[185] and of Taylor[186] on the production of toxin on simplified media and the recently reported successful purification of tetanus toxin[187] should lead to the preparation of toxoids possessing but a minimal capacity to induce sensitization phenomena. Meanwhile, many reports of successful and virtually reaction-free tetanus toxoid immunizations, including large numbers of allergic subjects,[140, 141, 144, 148, 154, 174–176, 180, 188, 189] suggest that the danger of allergic reactions in atopic subjects is no greater than that in normal persons — in marked contrast to the danger of using antitoxin in such subjects.

Indications for immunization. The indications for the employment of tetanus toxoid have been well summarized,[190] as follows: in allergic persons or those with known sensitivity to horse serum; in farmers, hostlers, veterinarians, horsemen and others experiencing relatively frequent opportunity for contamination of wounds with tetanus spores; and by and large in children, among whom the incidence of infected wounds is high and many unnoticed infections may result in tetanus. The combination of tetanus toxoid with diphtheria toxoid for immunization of children therefore appears wise not only in private practice but also as an adjunct to diphtheria-control programs.

The best type of schedule might well be adapted from that of the United States Army[35]: primary immunization with two doses of APT or three of FT at intervals of one month or longer, followed by at least one recall dose six to twelve months later and another recall dose after any injury of the sort that is known to involve the risk of tetanus infection. The available evidence suggests that active immunity is acquired within two weeks after the primary immunization is completed, but it is nevertheless wise to heed the warning of Tuft[191] and carry out immunization so far as practicable in advance of possible exposure to tetanus. The practice of administering prophylactic antitoxin routinely following accidents or injuries will have to be greatly modified in civilian practice. When such injuries occur to persons who are known to have been actively immunized, such as all veterans of World War II, emergency prophylaxis should be obtained by administering a booster dose of toxoid.[192]

(To be continued)

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192. Freedman, A. Tetanus immunization. *J. A. M. A.* **129**:1045,1945.

NEW HAMPSHIRE MEDICAL SOCIETY

PROCEEDINGS OF THE ONE HUNDRED AND FIFTY-FIFTH ANNIVERSARY

House of Delegates, May 13 and 14, 1946

THE House of Delegates convened at the Hotel Carpenter, Manchester, on May 13, 1946, at 7:30 p.m., with Speaker Deering G. Smith presiding. The following members answered the roll call:

The President, *ex-officio*
The Vice-President, *ex-officio*
The Secretary-Treasurer, *ex-officio*
Samuel Feiner, Ashland
Earl J. Gage, Laconia
Francis J. C. Dube, Center Ossipee
W. J. Paul Dye, Wolfeboro
Albert C. Johnston, Keene
James M. Ballou, Keene
Marjorie B. Parsons, Colebrook
Francis M. Appleton, Gorham
Howard N. Kingsford, Hanover
Israel A. Dinerman, Canaan
Leslie K. Sycamore, Hanover
Robert E. Biron, Manchester
George C. Wilkins, Manchester (alternate for Samuel Fraser)
Loren F. Richards, Nashua
Robert R. Rix, Manchester
Deering G. Smith, Nashua
Frank J. McQuade, Franklin
William P. Clough, Jr., New London
Philip M. L. Forsberg, Concord
Willard C. Montgomery, Epping
Samuel T. Ladd, Portsmouth
Robert W. Tower, Plaistow
William R. Latchaw, Somersworth
Raymond R. Perreault, Rochester
Addison Roe, Newport
B. Read Lewin, Claremont

The Speaker declared a quorum present, and appointed the Credentials Committee as follows: Drs. Appleton, Latchaw and Feiner. To the Committee on Officers' Reports, he appointed Drs. Lewin (chairman), Biron and Montgomery. To the Committee on Communications and Memorials he appointed Drs. Dinerman, Tower and Perrault. To the Committee on Nominations, he appointed Drs. Richards (chairman), Gage, Forsberg, Dye and Ladd. For the Committee on Credentials, Dr. Appleton reported that the credentials were in order.

On motion duly made and seconded, it was voted to omit the reading of the previous minutes, because of the publication of the proceedings.

On motion duly made and seconded, it was voted to dispense with the reading of the reports of the councilors, since they will be published in the *Transactions*.

The Secretary-Treasurer, Dr. Carleton R. Metcalf, presented his report, as follows:

Membership, December 31, 1945

PAID

Belknap County	23	
Carroll County	9	
Cheshire County	17	
Coos County	21	
Grafton County	58	
Hillsborough County	98	
Merrimack County	53	
Rockingham County	46	
Strafford County	29	
Sullivan County	14	
Not in County Society	3	
		371

UNPAID

Life members	18	
Honorary members	5	
Members in service and delinquents	134	
		157
		528

The total membership on December 31, 1944, was 546.

Financial Statement

RECEIPTS

January 1, 1945 — balance forward	$677.42
Belknap County	156.00
Carroll County	66.00
Cheshire County	78.00
Coos County	156.00
Grafton County	342.00
Hillsborough County	588.00
Merrimack County	348.00
Rockingham County	282.00
Strafford County	174.00
Sullivan County	84.00
Cash received at annual meeting	119.00
Members not in county societies	18.00
Refund (Cancer Committee)	18.80
Donations to National Physicians Committee (Merrimack County, $50; Strafford County, $29; Sullivan County, $14)	93.00
Benevolence Fund (Hillsborough County)	40.00
	$3240.22

EXPENDITURES

New England Journal of Medicine:	
Journals	$483.93
Transactions	1168.46
Tables	4.23
Carleton R. Metcalf (salary)	500.00
Printing	104.00
Envelopes and stamps	47.17
Halftone cuts	28.90
Clerical work	111.50
Telephone and telegraph calls	19.77
Retaining fee	100.00
Guest speakers (fees)	26.93
Cancer Committee	40.00
Cash collected at annual meeting	77.00
Benevolent Fund:	
Hillsborough County	40.00
Merrimack County (received in 1944)	20.00
National Physicians Committee (donations):	
Merrimack County	50.00
Strafford County	29.00
Sullivan County	14.00
Strafford County (received in 1944)	28.00
Madeline A. May (stenographer at annual meeting)	226.87
Flowers (H. O. Smith)	12.38
Service charges at bank	.84
	$3132.98
Balance, January 1, 1946	107.24
	$3240.22

The total membership on December 31, 1945, was 528. This is a decrease of eighteen over the preceding year.

The following officers died during the year 1945: Clifton S. Abbott, Laconia; Henry O. Smith, Hudson; Herbert L. Taylor, Portsmouth; and Richard E. Wilder, Whitefield.

Although no money was added to the Benevolence Fund from the annual dues during 1945, a donation was received from the Hillsborough County Auxiliary. Ninety-three dollars for the National Physicians Committee was received from the following auxiliaries: Merrimack County, Strafford County and Sullivan County.

In accordance with instructions from the House of Delegates, $40.00 was given to the Cancer Committee. The question of outpatient psychiatric care in New Hampshire was referred to the Committee on Mental Hygiene, with the request that it consider the matter and report at this meeting.

A report on the New Hampshire Physicians' Service, or Blue Shield, which was inaugurated and sponsored by the House of Delegates, will be given by its president, Leslie K. Sycamore.

I recommend that we drop the following two standing committees this year: the Committee on O.P.A. Assistance and the Committee on Medical Preparedness. On the other hand, we should add one new standing committee because during the last year the Council of the State Medical Societies of New England has been rejuvenated. This council held three or four meetings and considered medical matters that pertained to all the New England states, particularly matters of national legislation. Dr. Robinson, Dr. Sycamore and I attended two meetings as unofficial delegates from New Hampshire and we gave the Council $100.00 from the treasury of this society to help pay the running expenses. I suggest that the House of Delegates approve this fee and apportion $100.00 each year for the same purpose and that the Committee on Nominations recommend a standing committee of three for membership on this council. Now that many of the members of this society have returned from the Armed Services, I also suggest to the Committee on Nominations that our various committees be strengthened by the appointment of a due proportion of younger men and of veterans. The Committee on Nominations should also note that Dr. Fitch has resigned as alternate delegate to the American Medical Association.

The annual meeting this year is limited to one day for two reasons: it is difficult to get hotel accommodations to stay overnight in Manchester; and a one-day meeting is less expensive than a longer meeting and we have been "in the red" for the last few years. I hope, however, that next year and thereafter we may return to our former plan of having the annual meeting last for two days. Some members of the Society have suggested that the meeting next year be held during June at one of the resort hotels, for example, a hotel at Portsmouth or one at Sunapee. A scheme of this sort has been followed for many years by the Maine Medical Association, whose members seem to like it. I recommend that the House of Delegates give it consideration.

In view of our somewhat embarrassed financial position, I recommend an increase in the annual dues of the Society. The present by-law reads "an assessment of $6.00 per capita on the membership of the component societies is hereby made the annual dues of this society." If this assessment were increased to $9.00, we should be able to carry on much better in an era in which expenses have slowly but surely become greater. Such an increase would presumably mean that each member of the county society would pay $10.00, of which $1.00 would be retained in the county and $9.00 turned over to this organization. I have referred this matter to the Committee on Amendments. If it meets with the approval of this committee and your approval, the amendments should first be made in the House of Delegates and then ratified by each county society.

It is of interest to note that the Vermont State Medical Society has recently raised its annual dues to $20.00, so that the increase that I have suggested seems relatively modest.

At the present time, the *New England Journal of Medicine* has been sent to each of our members once a month. Recently the *Journal* has suggested a modification of the arrangements as follows:

Either one of two arrangements is possible. The first is to send *all issues* of the *Journal* to the members of your society at a charge of $2.50 for the current year. This, of course, would probably mean an increase in the annual dues of $1.50. On the other hand, it seems likely that your members would derive a reasonable amount of benefit. The second is to continue with the present arrangement so far as all members of your society are concerned, but to permit any member to subscribe individually for *all issues* at an extra cost of $1.50.

So far as the future is concerned, the rate of $2.50 cannot be guaranteed. It seems reasonably certain, however, that there will not be an appreciable increase in cost, and if the circulation continues to increase and the advertising revenue is maintained, it might well be lowered.

At the present time the Society pays the *New England Journal of Medicine* $1.00 a year for each member.

I should recommend the second alternative: continue the present arrangement, but permit any member who wishes all issues to procure them by sending a check of $1.50 directly to the *Journal*.

At the time this report is being written, the Wagner–Murray–Dingell Bill is being considered by the Committee on Education and Labor of the United States Senate. In accordance with the instructions passed by the House of Delegates, the Committee on Public Relations has been active in opposing this legislation.

Dr. Robinson and I spent two days last February at a meeting of the National Physicians' Committee in St. Louis, where this and other federal legislation was thoroughly discussed. Here in New Hampshire, through the press and through personal contacts with various groups, we have tried to present the point of view of the Society, and many of these groups have co-operated with us in expressing their disapproval to our Congressional delegation. The end result is that as this report is written Senator Bridges, Congressman Adams and Congressman Merrow have stated that they would vote against the present Wagner Bill. Senator Tobey has been noncommittal.

On motion duly made and seconded, it was voted that the report of the Secretary-Treasurer be referred to the Committee on Officers' Reports.

Dr. Lewin, chairman of the Committee on Officers' Reports, then stated that the Committee on Officers' Reports had recommended that the Nominating Committee create a new standing committee of three members, to be called the Committee of New England Medical Societies. He moved the adoption of this portion of the report. The motion was duly seconded.

The President expressed some doubt whether a new committee could be created by the Nominating Committee, since this was a matter of the by-laws of the Society and would require an amendment.

Dr. Dye stated that the various standing committees came under the by-laws and the constitution, and that such a motion could therefore be recommended one day, put on the table that night and voted on the following day. He recommended such an amendment.

The Speaker requested the Secretary's opinion.

The Secretary replied that it was much easier to have all the committees on the same basis, and that they could be changed when necessary.

The President stated that he saw no reason why a special committee could not be appointed.

The Speaker asked for the motion again.

Dr. Lewin moved that the House of Delegates instruct the Nominating Committee to create a new standing committee of three members, to be called the Committee of New England Medical Societies.

Dr. Dye moved that Chapter VIII of the by-laws be amended to include the committee recommended by the Committee on Officers' Reports. This motion was duly seconded.

Dr. Lewin moved that the House of Delegates approve the $100.00 given to the Council of the State Medical Societies of New England during this last year. This motion was duly seconded and carried.

Dr. Lewin then moved that $100.00 be appropriated for the Council of the State Medical Societies of New England this year.

This motion was duly seconded and carried.

Dr. Lewin stated that the Committee on Officers' Reports had reached no conclusion regarding the site of future meetings. He recommended open discussion by the delegates.

Dr. Sycamore stated that the delegates from Grafton were instructed to change the meeting place next year and asked whether such a decision were the province of the Program Committee.

The Speaker replied that the matter was one for decision by the House of Delegates.

Dr. Sycamore moved that the House of Delegates be empowered at least to investigate another site for a meeting for next year and to adopt another site if a suitable one were available.

The Secretary observed that the situation has been complicated by transportation and by hotel accommodations, with practically no rooms available in Manchester. If a two-day meeting were held, the members who lived at a distance would probably have to come for only one day. The thought in suggesting this matter was that the Society could meet in some place like the Wentworth in Portsmouth. He further stated that the Wentworth advertises for conventions, which they can accommodate any time after June 1. He added that the housing problem would be solved at the Wentworth.

The Speaker asked if there was any further discussion on this subject.

Dr. Ladd believed that the Wentworth would be a desirable place for the meeting.

The Speaker called attention to the fact that the by-laws state that the Society shall hold an annual session, during which there shall be held daily not less than two general meetings open to all registered members, delegates and guests, and that the place for holding such annual session shall be fixed by the House of Delegates, and the date by the President and the Secretary-Treasurer.

Dr. Wilkins moved that the next meeting be held in Portsmouth at the Wentworth.

The motion was duly seconded by Dr. Dye.

The Secretary suggested that power be given to someone to select a place, so that if the Wentworth burned down a special meeting would not have to be called.

Dr. Wilkins accepted the amendment.

The Speaker asked for the opinion of those who wanted a two-day meeting. There was a unanimous showing of hands. He then stated that the motion before the House was that the next meeting of the Society should be held at the Hotel Wentworth in Portsmouth, and that if that site were not available, the President, together with the Vice-President and the Secretary, would select the site. The motion was carried.

Dr. Lewin, for the Committee on Officers' Reports, moved that the present arrangement, namely, that the Society pay the *New England Journal of Medicine* $1.00 a year for each member be continued, but that any member who wished all issues of the *Journal* obtain them by sending a check for $1.50 directly to the *Journal*.

This motion was duly seconded, and was carried.

Dr. Lewin, for the Committee on Officers' Reports, then moved that Dr. Metcalf's report be accepted in full.

This motion was duly seconded and was carried.

Dr. Paul Dye for the Committee on Amendments to the Constitution and By-Laws, made the following recommendations: to amend Article IV, Section 1, of the constitution, to read as follows: "This society shall consist of members, life members and honorary members"; to amend Section III, Article 4, to read as follows: "life members shall be those members whose dues are remitted."

Dr. Dye stated that these changes had been accepted unanimously by the House of Delegates in 1945 and presented in open meeting at the annual session, and should therefore come up for a final vote at the 1946 meeting.

Dr. Dye also recommended that Section 1 of Chapter 10 of the by-laws be amended to read as follows: "An assessment of $9.00 per capita on the membership of the component societies is hereby made the annual dues of this society." He pointed out that this provision meant that each county society should charge $10.00 for its membership, retaining $1.00 for itself and sending $9.00 per member to the New Hampshire Medical Society; presumably, each county society would have to take similar action under its by-laws to cover these increased dues.

The Speaker stated that although this matter was presumably to be laid on the table for discussion until the following morning and although no formal action could be taken immediately, it might be wise to discuss it.

A member inquired if $3.00 were a sufficient increase.

The Secretary stated that this increase would raise the dues enough for the coming year, and recommended such an increase, which could be raised further if great expenses were incurred.

Dr. Biron recommended raising the dues to $10.00, which would pay an assessment in toto of $11.00.

The Speaker stated that Hillsborough County had added an assessment of $1.00 to the dues this year, and that every man except one had paid the $8.00 rather than $7.00.

The Secretary pointed out that any excess, no matter what the dues were, was turned back to the Trustees. Up to the beginning of the war, something was returned every year for the General Fund; since the beginning of war, money had been borrowed from the Trustees at the rate of $500 to $1000 a year.

Dr. Wilkins proposed that the dues be increased to a figure that would be sufficient to support the activities of the Society, believing that if the dues were $12.00, or anything above $10.00, such an amount would be better than $9.00.

The Speaker requested that all those in favor of raising the dues raise their right hands.

The decision to increase the dues was unanimous.

The Speaker then asked how many wanted the dues raised to $9.00 or $10.00.

Dr. Montgomery inquired if there were any objection to raising the dues to $14.00, making the total $15.00.

The Speaker asked how much money had been withdrawn from the General Fund.

Dr. Wilkins replied that $500 had been withdrawn and that he believed that more than $500 had been withdrawn during the previous year.

It was asked how much money was in the General Fund.

Dr. Wilkins replied that there was $4957.74 in the General Fund — a much smaller amount than had been in the Fund a few years previously because during the war the general reserve funds that had been established had been depleted to help the general running expenses of the Society.

The Speaker stated that the reserve fund could be drawn on, if necessary, whereas the other funds, like the Benevolence Fund, could not be touched.

The Secretary said that nothing had been given to the Benevolence Fund for the last three or four years.

The Speaker asked that all those in favor of $14.00 a year raise their hands. Sixteen hands were raised. He then requested those opposed to $14.00 per year to raise their hands. Seven hands were raised.

Dr. Clough stated that on the basis of 528 members in the Society, $2500 would be put into the General Fund; approximately $1500 had been withdrawn in the war years, and $2500 would be replaced. He asked for an explanation why that amount was needed in the General Fund.

Dr. Lewin, as secretary of the Sullivan County Medical Society, expected to encounter some difficulty in collecting $15.00, and believed that many of the members would greatly object.

Dr. Sycamore stated that many members of the Society discharged from the armed forces might have some difficulty in meeting various extra expenses that returning to civilian life entails. He suggested that the dues might be raised sufficiently

to cover expenses for the year and that the following next year, if necessary, the dues be increased again.

Dr. Ladd invited attention to the fact that the $15.00 could be deducted from income taxes, and stated that in his county the reserve fund had mounted to around $400 or $500.

A question was asked if the General Fund were a fund to be drawn on during the war years and if there were any other functions of the fund.

The Speaker replied that the Secretary had informed him that there was no other function of the General Fund, except as a reserve fund.

Dr. Wilkins stated that it was the General Fund that has been built up. Analysis for seven or eight years had revealed that the New Hampshire Medical Society was not self-supporting: the money received and the money paid out for various expenses required $500 a year more from the general fund. The dues collected did not carry or cover the cost of the running of the Society, and in a year in which no money was received from the exhibitors there had been a large deficit; a similar deficit had occurred in the previous two or three years, with only a one-day meeting and with a decrease in the amount received from the exhibitors. To meet expenses, the dues of the society must be raised at least $1.00.

Dr. Biron inquired whether, when the Secretary made his estimate, he considered that such a sum would not only carry the annual meeting for the next year but also perhaps repay some of the loan received from the General Fund. If so, Dr. Biron believed that the estimate should be considered sufficient.

The Secretary replied that he did not know exactly how much, if anything, could be paid back, but that the Society could get by on a rate of $10.00.

Dr. Wilkins pointed out that the Society had always been in the position of being partially supported by the exhibitors. He believed that the Society should be able to support itself.

Dr. Montgomery remarked that a two-day meeting would cost more than $1.00, and more than the $5.00 or $6.00 that was being asked as an increase.

Dr. Ladd stated that speakers from outside the State cost $100.00 each and that expenses were high.

The President expressed his opinion that the dues should be increased sufficiently to meet the expenses of the Society, but saw absolutely no reason for making the dues any higher than necessary. Until the war, the Society had always had a two-day meeting, and the reports of the Treasurer for a number of years in normal times, even on the former rate, showed that there was enough money to add a little to the General Fund, which had no specific purpose and therefore no object for being built up. The money had not been loaned with the idea that it has to be paid back. This was an emergency fund. Consequently, the President was in favor of a reasonable amount such as $12.00, but not $14.00, and preferably $10.00. The Vermont State Medical Society was said to have raised its dues to $20.00, but that increase was necessary because a full-time executive secretary was employed.

The President observed that at meetings of the House of Delegates, year after year, delegates gave a good deal of their time and consideration to particular problems that were presented to the Society. In the following year, the minutes of the previous meetings of the House of Delegates, as is customary, were always left unread. The *Transactions* of the Society were printed in the *New England Journal of Medicine*, some in one issue and some in following issues, and as a rule were not read by most members. He believed that if the minutes of the meetings could be read, much of the discussion would be unnecessary. He added that some committee of the Society could profitably make a search through the minutes of the House of Delegates for the last six years, because the time saved and duplication avoided would tend to give a progressive structure to the deliberations of the House of Delegates.

The Speaker stated that the minutes of the previous meeting occupied about forty-five pages of the *Transactions* and would take about two hours to be read.

The President said that if a member or a committee could bring to the House of Delegates a summary of the actions taken, and a report of whether the will of the Society had been carried out, the whole procedure would be much improved.

Dr. Dye stated that a small addition to the Secretary's estimate of $9.00 would probably ensure sufficient funds for the operation of the Society. He therefore moved that the annual dues of the Society be raised to $10.00.

This motion was duly seconded by Dr. Dinerman, and on a showing of hands, the opinion was unanimous, although no official vote was taken.

Dr. Dye then announced that he would submit the vote for the amendment at the meeting on the following morning.

Dr. Lewin, in the absence of the chairman, read the report of the Committee on Child Health, as follows:

> The Committee on Child Health has been relatively inactive. A most important step toward the betterment of the health of the children of New Hampshire is the study of child-health services of the American Academy of Pediatrics, which is now in progress. We urge the cooperation of all the members of the Society in this study.
>
> COLIN C. STEWART, *Chairman*
> B. READ LEWIN
> FRANKLIN ROGERS

Dr. Lewin moved that this report of the Committee on Child Health be accepted.

This motion was duly seconded.

The President stated that a physician from Massachusetts engaged in work of a similar nature to that reported would present a résumé on the child-

health survey by the American Academy of Pediatrics at the general meeting on the following day.

It was moved and seconded that the report of the Committee on Child Health be accepted; the motion was carried.

The report of the Committee on the Control of Cancer was then presented by the chairman, Dr. George C. Wilkins:

Last year, the House of Delegates approved a suggestion of this committee that a cancer-instruction day be offered to general practitioners of the State. During April, which is cancer-control month, such a meeting was held at Manchester. A program of thirty-minute talks on the diagnosis and treatment of eight different forms of cancer was presented by five New Hampshire surgeons and three surgeons from Boston. These talks were interesting and stimulating, but the committee received slightly less than one hundred acceptances and some of those accepting did not attend. Furthermore, the men who did attend were mostly the ones who are progressive, well informed and always attend medical meetings. The committee feels a certain amount of disappointment that there were not in attendance more rural and urban general practitioners who see few cancer cases but on whom the fate of a patient with cancer chiefly depends. Your committee intends to plan another meeting next year. The expenses of the meeting, including an excellent lunch, were borne by the Field Army of the American Cancer Society.

Since our last report, two physicians attached to the cancer clinics have taken advantage of the aid given by the Field Army for refresher courses. We hope and expect that more will take advantage of this opportunity, now that so many physicians have returned from the services.

High-school education in cancer control has greatly increased. Last year, the schools in Manchester, where the experiment was initiated, asked for its continuance. Last September, with the active co-operation of the Commissioner of Education, the instruction pamphlets and teachers' guides were offered to all the high schools of the State. At the present time, over 60 per cent of the high schools are using the instruction pamphlets in the science classes. This development has been the responsibility of the Field Army, aided by your committee.

The Cancer Commission and its fourteen clinics have continued to function smoothly. Some clinics have few patients and some have many, but it has been found that the usefulness of a clinic depends chiefly on the interest, ability and enthusiasm of its director. During the past year, 1441 patients attended the clinics, of whom 592 were new patients and 849 were making return visits. Of the new patients, 51 per cent were found to have cancer.

There is continued evidence of the need of public education in the early signs of cancer, and of the value of early treatment, especially among people of the middle and older ages. The younger generation accept it more readily, and therein lies our hope of good results from continual educational efforts.

Your committee sent three short letters to all physicians in the State. One, entitled "Breast Tumors," urged the removal of all definite tumors of the breast and cited tumors as small as 5 mm. that were definitely malignant. In the presence of breast tumor one should never advise "let it alone." Another letter discussed "The Significance of a Negative Biopsy Report," and explained why and how errors could be made. It was suggested that in all questionable cases a conference between the surgeon and the pathologist is always advisable. Our last letter described the usual locations of skin cancer, the usual types found, and suggestions regarding diagnosis and treatment, particularly stressing that any new growth on the skin of a patient over forty years of age should be considered malignant until proved otherwise.

Your committee recommends increasing the Committee on the Control of Cancer to five members and asks the House of Delegates to instruct the Nominating Committee to add two names.

Your committee has expended the entire amount appropriated last year. On account of the increased cost of printing and a larger number of physicians, we request the sum of $60.00 for next year's expenses.

GEORGE C. WILKINS, *Chairman*
RALPH E. MILLER
GEORGE F. DWINELL

Dr. Lewin, for the Committee on Officers' Reports, recommended that the Committee on the Control of Cancer be increased to five members. This motion was duly seconded.

Dr. Dye expressed the opinion that his committee would be in agreement that Section 11 of Chapter VIII of the by-laws be amended and that the Committee on the Control of Cancer be increased to five members, and therefore moved that this recommendation be laid on the table, to be voted on at the meeting on the following morning.

This motion was duly seconded and was carried.

Dr. Lewin, for the Committee on Officers' Reports, moved that the sum of $60.00 for the Committee on the Control of Cancer be approved. This motion was duly seconded and was carried.

Dr. Lewin, for the Committee on Officers' Reports then moved that the report of the Committee on the Control of Cancer be accepted and that Dr. Wilkins be commended for his unceasing efforts to improve cancer diagnosis and treatment throughout the State. This motion was duly seconded and was carried.

The report of the Committee on Maternity and Infancy was then read, as follows:

Each year the Committee on Maternity and Infancy of the New Hampshire Medical Society conducts a study on the maternal deaths, infant deaths and stillbirths reported for the calendar year previously ended. This study is for mortality reported for the year 1945. As in the past, the committee has endeavored to obtain as full data as possible on each death, analyze, and so far as possible appraise and come to conclusions on the material submitted by physicians in their answers to questionnaires. It should always be borne in mind that infallible judgment is impossible and that conclusions drawn are to be interpreted in the light of objective observers looking into a situation after the event has passed and, in retrospect, appraising the conduct entering into the final result. The committee wishes to stress the fact that conclusions drawn are accurate only to the degree that data at hand are complete. Sometimes the information on a given case is scanty indeed, and it is urged that physicians and hospitals make a special effort to submit information as complete as possible.

It is planned that another year the committee will submit a more complete questionnaire designed to secure as full data as possible. It is hoped that such a device will aid greatly in making the study more complete.

The information for the study was gathered from the records of physicians and hospitals. All but one physician responded to the questionnaires, most cases having been reported with fair completeness. Assistance in gathering and compiling data was obtained through personnel of the State Department of Health, and as in the past the committee did not know the identity of the physician, patient or hospital when evaluating the facts presented by their agent.

The year 1945 was gratifying in that the maternal death rate decreased from that of the two previous years. The lowest rate was in 1942: 1.6 per 1000 live births. The rate in 1945 was 1.9 per 1000 live births. The number of ma-

ternal deaths was 16, with a slight decrease in the birth rate as compared with the previous year. There were 8551 births in 1945.

In the tabulations to follow, it is interesting that although most cases are classified as unavoidable, a greater number of cases were regarded as having received inadequate treatment than in previous years. Of the 16 deaths, the method of delivery reported for 8 of the cases was operative or "forced." The committee cannot stress too often the opinion that there is never any justification for an *accouchement forcé*.

In the twelve years during which this study has been conducted, the high point was reached in 1935, with a rate of 6.1 per 1000 live births, with 46 deaths. At this point it was easy to speculate that improved obstetrics, increased knowledge, better facilities of both hospitals and physicians and intensified programs for fostering better maternity care were responsible for a lower trend, and such factors may well have been responsible. The maternal death rate rose sharply in 1943, however, and continued to climb in 1944. These being war years, the scarcity of personnel, stresses of wartime and fewer facilities, especially in hospitals, may well have been to blame. Now that 1945 has written its page in history, it is truly encouraging to note the decrease in the maternal death rate.

The committee did not attempt to do an intensive study on infant deaths under one year, or of stillbirths; time and personnel were not available for such a study. Tabulations regarding causes of infant deaths, however, follow. Again the committee includes in this report the definition of a stillbirth that has become accepted in most states. There will always be some confusion in the reporting of stillbirths because of individual interpretations, especially since the period of gestation that must be reached before registration as a stillbirth, differs in many states.

Maternal Deaths

In 1945, the period of this study, there were 16 maternal deaths. The number of live births was 8551. This gives a rate of 1.9 per 1000 live births. Since 1941, the birth rate has steadily climbed, probably because of an influx of population into defense areas and more marriages among servicemen. All deaths reported occurred in hospitals.

The following is a tabulation of maternal deaths by cause for the year 1945 as established by the committee and subdivided according to causes of death as assigned by the Division of Vital Statistics in accordance with the *International List of Causes of Death* (fifth edition):

CHIEF CAUSE ACCORDING TO INTERNATIONAL CODE	NO. OF CASES
Other accidents of pregnancy and specified conditions of childbirth (including death before delivery)	6
Hemorrhage of pregnancy (including death before delivery and those of puerperium)	3
Infection during childbirth and puerperium	3
Abortions	2
Puerperal toxemia	2
Total	16

CHIEF CAUSE AS CLASSIFIED BY COMMITTEE	NO. OF CASES
Puerperal emboli	4
Ruptured uterus	3
Toxemias (all types)	3
Myocardial failure	2
Nonmaternal	1
Hemorrhage of childbirth	1
Unknown (incomplete data)	2
Total	16

CAUSE OF DEATH	NO. OF DEATHS AS ASSIGNED BY INTERNATIONAL CODE	NO. OF DEATHS AS GROUPED BY COMMITTEE
Puerperal emboli		4
Abortion	1	
Other diseases and accidents of pregnancy (death before delivery)	1	
Infection during childbirth and puerperium	2	
Ruptured uterus		3
Other accidents and specified conditions of childbirth	1	
Hemorrhage of pregnancy (death before delivery)	1	
Hemorrhage of childbirth and puerperium	1	
Myocardial failure		2
Other accidents and specified conditions of childbirth	1	
Other diseases and accidents of pregnancy (death before delivery)	1	
Toxemias (all types)		3
Puerperal toxemia	2	
Infection during childbirth and puerperium	1	
Hemorrhage of childbirth and puerperium	1	1
Incomplete		2
Other accidents and specified conditions of childbirth	2	
Nonmaternal deaths		1
Abortion	1	
Total	16	16

In the 16 fatal cases 5 cesarean sections were performed. The causes of death recorded were as follows: toxemia 2; post-partum hemorrhage 1; ruptured uterus 1; and unknown 1.

In 3 other cases a forced delivery was performed, and the committee interprets such procedures as referring to an *accouchement forcé*. These reports reveal that almost half the deaths studied (8 cases) involved operative or forceful means of delivery, only 2 of which, in the opinion of the committee, were indicated because of either a previous section or an apparent disproportion. The committee cannot justify any cause for a forced delivery.

One case to illustrate a forced delivery occurred when the attending physician during the course of a normal labor in a twenty-three-year-old multipara observed that the fetal heart was accelerated. He became alarmed and called in a consultant. From the data obtainable on the report, it appeared that, with the cervix dilated but one finger-breadth, the consultant performed what was recorded as a forced delivery, obtaining a stillborn child. The placenta showed some infarcts. The fact that some blood clots were observed led to a diagnosis of abruptio placenta, which was given as a cause of death. The patient went into shock following delivery and expired. The committee believes the diagnosis to be incorrect from the data, but believes that the patient died as a result of the treatment, presumably from a ruptured uterus resulting from the forced delivery. It is to be remembered that this conclusion was reached from the material at hand. Whether the membranes had ruptured previously was not known, and it was not recorded whether the patient was examined after death for ruptured uterus.

It has been the usual procedure for the committee to classify these deaths further, to illustrate if possible where the responsibility for maternal deaths belongs. The groups are as follows: Group 1, 2 cases in which the patient was at fault because of refusal of prenatal care, neglect and so forth (1 case of obesity and myocardial failure, and 1 of eclampsia); Group 2, 4 cases in which the obstetric treatment was apparently inadequate (3 cases of ruptured

uterus, and 1 of post-partum hemorrhage); Group 3, 7 deaths that were apparently unavoidable (3 cases of eclampsia, and 4 of pulmonary emboli); and Group 4, 2 cases in which data were insufficient and the cause of death was therefore undetermined (1 case of postoperative pulmonary emboli, and 1 of myocardial failure).

In 1 case in Group 3 in which the cause of death was reported as post-partum hemorrhage, the committee believed that treatment was inadequate. The patient went into shock following a cesarean section, and no intravenous therapy, particularly plasma, was administered for at least forty-five minutes, although the anesthetist was aware of the patient's condition. The committee considered the cause of death to be surgical shock rather than post-partum hemorrhage, especially since there was no evidence of excessive bleeding. It was further believed that an anesthetist should take the initiative in ordering shock therapy, especially when the attending physician has his hands full with delivery or surgery.

Maternal mortality rates per 1000 live births by years were as follows: 1933, 6.3; 1934, 5.4; 1935, 6.1; 1936, 4.8; 1937, 4.3; 1938, 3.8; 1939, 3.1; 1940, 3.1; 1941, 1.9; 1942, 1.6; 1943, 2.4; 1944, 2.9; and 1945, 1.9.

The deaths by counties in 1945 were: Belknap, 1; Hillsborough, 6; Strafford 5; Coos 2; Cheshire 1; and Rockingham 1.

Infant Deaths

The following is a list of the ten chief causes of death recorded for infants under one year of age. In 1945 there were 299 deaths from all causes — a rate of 35 per 1000 live births. In order, the causes were prematurity, congenital malformations, birth injuries, other diseases peculiar to first year of life, lobar pneumonia, pneumonia (other), accidental suffocation, diarrhea and cerebrospinal meningitis. It should be noted that the chief cause of death listed is premature birth. The Committee believes that this should not be considered a cause of death and that better and more adequate treatment and facilities for the care of premature infants should be stressed. Maintenance of body temperature and thorough nursing care, including proper feeding, is essential.

Stillbirths

In 1945 200 stillbirths were reported — a rate of 23.4 per 1000 live births. The causes were varied and substantially unrevealing. Again the committee prints the accepted definition of a stillbirth, as follows: "A fetus showing no evidence of life after complete birth (no action of heart, breathing or movement of voluntary muscle), if the twentieth week of gestation has been reached, should be registered as a stillbirth." For the most part the causes of fetal death as given on death certificates are maternal conditions, with the exception of fetal deformities. Here again the classification of causes of stillbirths varies. The International Commission for Revision of the International List of Causes of Death in 1938 adopted the following classification, which is given here in outline only: stillbirth caused by disease in, or accident to, the mother; anomalies of the fetus, placenta or cord; death of the fetus from injury or other causes; and stillbirth due to other causes. In a diagnosis of causes of death, the foregoing should be kept in mind.

Comments and Recommendations

By way of summary and to emphasize examples of apparently poor obstetrics, the committee wishes to point out the following facts and make some suggestions. It is hoped that the conduct of future deliveries may be favorably affected by constructive criticism. The cases of toxemia reported again illustrate that there is still a tendency to neglect the medical aspects of the condition by inadequate treatment. The majority of patients with toxemia reported this year were seen late in pregnancy, with symptoms of the toxemia apparent. The tendency has been to induce labor or perform a cesarean section without giving adequate medical care or preparation. The committee strongly urges the immediate treatment of toxemia by the use of magnesium sulfate in the early stages, early induction with due regard to prematurity, glucose and magnesium sulfate in severe cases and in eclampsia complete digitalization as soon as possible, with added use of glucose and oxygen if necessary. The magnesium sulfate, glucose and digitalization should be instituted immediately, pending the decision of the method or time of delivery. It is more important that the patient be treated than to empty the uterus.

The committee wishes to make a plea for a larger number of trained and skilled anesthetists. Many unfortunate incidents can be avoided if a trained anesthetist is constantly alert for symptoms of shock and is skilled in the administration or supervision of shock therapy. Almost every year a case is cited in which the failure of the anesthetist to act quickly or adequately leads to the patient's death.

It is urged that more autopsies should be sought. Frequently the correct diagnosis can be determined, especially in cases in which the cause of death is recorded as post-partum hemorrhage or shock. Post-partum hemorrhage may be due to retained cotyledons, ruptured uterus, cervical tears, fibromas and varicosities.

If hemorrhage is suspected, immediate search for such causes should be instituted. The committee emphasizes again the necessity of proper diagnosis and immediate treatment of patients with hemorrhage or who show signs of shock immediately or soon after delivery, whether delivery was spontaneous or operative. Plasma, now available to all free of charge, should prove an invaluable means of combating shock in such cases.

It is again stated that the committee cannot find justification for a forced delivery. In cases of transverse presentation it is possible that an external cephalic version could be attempted before labor has set in, and if the membranes are intact, the patient should surely be permitted to go to full dilatation before delivery is attempted. If the membranes have ruptured, the cervix is not dilated and the uterus is dry, an internal podalic version is definitely contraindicated. A better alternative is cesarean section.

The committee wishes to comment on the value of qualified consultation in obstetrics emphasizing that the consultant's prerequisites should include ample experience in obstetrics and not merely skill in surgery.

If the committee is to make fair and helpful suggestions, based on conclusions reached in this study, it is essential that better reporting of the facts be practiced by physicians, since the committee has nothing to go on except information submitted.

The committee wishes to thank physicians and hospitals for reports completely and painstakingly filled out, as well as all physicians who co-operated in preparing this report. Acknowledgment and thanks are also expressed to the State Department of Health for its aid in compiling data and furnishing personnel.

Robert O. Blood, *Chairman*
Benjamin P. Burpee
Marion Fairfield

Dr. Lewin, for the Committee on Officers' Reports, commended the work of the Committee on Maternity and Infancy and moved that the report be accepted. This motion was duly seconded and was carried.

The report of the committee on Medical Economics was then presented by the Chairman, Dr. L. K. Sycamore, as follows:

For the last year, your committee has functioned mainly in the separate activities of its members, one of whom is president of the New Hampshire Medical Society, the chairman being president of the New Hampshire Physicians' Service. These activities occupied the time of the members to such an extent that any further functioning of the committee as a whole did not seem possible. Your committee has, however, considered the following subjects and presents its conclusions in this report.

Wagner–Murray–Dingell Bill

Your committee opposes the method of distribution of medical care proposed in the bill, believing that such a

program would be inefficient and ineffective, as well as detrimental to the best interests of patients. If government participation on the economic side of medical care is necessary through the establishment of any form of compulsory insurance, we favor the utilization of existing nonprofit insurance programs under the sponsorship of medical societies, government funds being used only to pay the premiums for the insured persons. The President is discussing this problem with the county societies throughout the year, and has actively registered his opposition to the Wagner–Murray–Dingell Bill through communication with the appropriate members of Congress and government officials.

New Hampshire Physicians' Service

Gratifying progress in growth has been made throughout the last year. There are now 36,000 participants in the Surgical Division, of whom 6000 are also covered under the Medical Division. This represents a fourfold increase over the enrollment a year ago.

Financially, the Corporation has accumulated sufficient reserves to permit the repayment of the original capital loan and the extension of coverage under both the surgical and medical contracts, with a reduction of the premium for the medical contract.

Studies are now being made on the coverage of veterans' care under a contract with the Veterans Bureau — a program already in effect in some other states — and on the coverage of indigent cases under a contract with the State Board of Public Welfare. Such coverage would materially increase the usefulness of the Service and would provide a valuable example of the possibility of co-operation in medical care between the government and the medical profession, with the control of the medical aspects remaining in the hands of the medical profession.

The whole-hearted co-operation of the members of the New Hampshire Medical Society in most areas of the State has been the key factor in the success of the Blue Shield program. Seventy-five per cent of the members are enrolled as participating physicians, the county enrollments running from 48 per cent to 98 per cent; seven counties have over 80 per cent enrollment. We need, however, the co-operation of the other 25 per cent to make the service fully effective. It is interesting to note that men returning from the armed forces are rapidly signing up as participating physicians. Constructive criticism has been helpful and has been gratefully accepted by the trustees of the New Hampshire Physicians' Service. Your committee wishes to commend the members of the New Hampshire Medical Society for their co-operation.

National Physicians' Committee

The National Physicians' Committee has organized a vigorous campaign against the Wagner–Murray–Dingell Bill, which undoubtedly has had considerable effect in arousing opposition throughout the nation. For this reason, the majority of your committee urges the New Hampshire Medical Society collectively and individually to support the National Physicians' Committee by encouragement and by financial aid.

The chairman is compelled to render a minority report in opposition to the methods employed, believing that the dogmatic propaganda broadcast by the National Physicians' Committee, employing on occasion apparently deliberate distortion and misrepresentation, will in the long run do a distinct disservice to the medical profession by cheapening the cause of medicine and by alienating the sympathies of the thoughtful layman.

Blue Triangle

The proposal of the New Hampshire Bankers' Association for physician-secured loans to patients for the payment of their medical bills was referred to the committee by the last House of Delegates. Your committee believes it is inadvisable to sponsor this proposal inasmuch as the Blue Triangle emblem of the plan would cause confusion with the Blue Shield and Blue Cross, and the plan itself to a certain degree would work at cross purposes with the voluntary insurance program.

L. K. Sycamore, *Chairman*
Francis J. C. Dube
R. W. Robinson

Dr. Lewin, for the Committee on Officers' Reports, stated that a new and interesting approach to government participation in medical care had been brought out by the Committee on Medical Economics: if the Government must participate in medical care, it should do so only to the extent of paying the premiums for the insured persons in some prepayment-insurance program under the sponsorship of medical societies. This would be good only if participation ended there. Dr. Lewin asked for discussion on whether there was agreement or disagreement with the Taft Bill as presented and whether the Government would co-operate in a prepayment plan under medical society sponsorship. He moved that the Society go on record as favoring government participation in a prepayment-insurance program under medical-society sponsorship. This motion was duly seconded.

The President, who had been in some measure associated with the development of this voluntary insurance plan in New Hampshire for some years, stated that his opinions had gone through all phases. Certainly, if the Government were to participate in this program, the only proper method was the supplying of the necessary means to cover the care given patients. The voluntary plans sponsored in the various states appeared to be the best course. He feared a very dangerous attack on the whole of the relation between patient and physician that any type of insurance or any agent assuming the cost of medical care for the patient might bring about. He pointed out that a patient must be required to make some sacrifice. He considered the local, voluntary plans much better than any compulsory insurance plan administered by anything as remote as the federal government.

In a small state like New Hampshire, the problems were close enough together for members of the professional committees of Blue Shield to regard the Blue Shield as the agent of the physician; consequently there was a definite reason for protecting it, to make its insurance successful. The President recalled a discussion two years previously regarding federal participation in medicine and whether it was impossible for the Government to collect moneys by taxation or otherwise and then to use the money for voluntary plans of insurance. The Government appeared to be interested in such a scheme.

The President further pointed out that one of the major objectives of interest in the voluntary-insurance plan was to provide some way not only of taking care of the medically indigent but also of devising a fee schedule to furnish some recompense at a time when the burden was tremendous. There had been a good deal of dissatisfaction with the system of treating the indigent under that fee schedule, which had been modified once. The President had had some discussions with the State Board of Welfare during the previous year and had suggested the State pay the insurance premium for indigent care;

at that time the President had stated that this presented simply one attitude. The medical profession had apparently agreed that this fee schedule was better than nothing, and that it was adequate recompense for the services rendered, provided that the State paid for the care. He pointed out, however, that physicians were selling their services to the State, for the care of the indigent, for a sum considerably less than the actual worth of those services, and that physicians must protect themselves and their ideals. There was no reason for the medical profession to give its service at a moderate fee, or at a cost lower than that of the grocer or other people dispensing commodities paid for by the State. Of course, laboratory and similar fees had not been included in the insurance plan, but it had been thought that such fees could be adjusted in the insurance scheme by accepting a type of service policy, including a complete service, the fees of the physician being kept on a detailed record form.

The President further stated that every case did not agree with Dr. Sycamore's minority report condemning the National Physicians' Committee.

Dr. Wilkins objected to the suggestion that the Society approved government participation in health insurance.

Dr. Lewin accepted the objection as an amendment.

The Secretary stated that in anticipation of this discussion he had sent a telegram to the American Medical Association asking its attitude on such proposals as the Taft Bill, and that the American Medical Association had replied that such proposals had not yet been considered officially. The Secretary questioned whether the House of Delegates should make any decision until the policy of the American Medical Association was known.

Dr. Clough agreed that decision on the program should be postponed, pending the opinion of the American Medical Association. Since the Blue Shield had been created to combat any interference by the Government in the practice of medicine in New Hampshire, Dr. Clough believed that it would be wiser to say nothing for the present but to consider the matter at greater length.

Dr. Ladd stated that if the motion were passed as read, the sponsors of the Wagner–Murray–Dingell Bill would at once say that the State of New Hampshire favored their bill. He therefore agreed that the wisest course was not to take any action until the attitude of the American Medical Association had been determined. He moved that the motion be laid on the table. This motion was duly seconded and was carried.

Dr. Lewin, for the Committee on Officers' Reports, moved that the House of Delegates not sponsor the Blue Triangle Plan of the New Hampshire Bankers' Association. This motion was duly seconded and was carried.

Dr. Lewin, for the Committee on Officers' Reports, then moved that the report of the Committee on Medical Economics be accepted. This motion was duly seconded and was carried.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 32341

PRESENTATION OF CASE

A forty-seven-year-old shipping clerk entered the hospital because of chronic cough.

The patient had been in apparent good health until a year before entry, when he developed a nonproductive cough, which he at first attributed to an upper respiratory infection but which persisted throughout the winter and became worse in the spring, with the development of some mucoid sputum. A physician prescribed pills that controlled the cough fairly well until the time of admission. The sputum had never contained blood or pus, and the patient denied any real pain, although he had some suprasternal and substernal soreness. He had noted no fever, but was told by his physician that he ran a slight temperature. Since the beginning of the illness he had lost 65 pounds, although his appetite had remained good.

Physical examination revealed a 2.5-cm. rubbery, superficial lymph node in the right supraclavicular region, just beneath the edge of the platysma muscle, and several deeper nodes in the right supraclavicular region. The heart and lungs were completely normal. Examination of the abdomen was negative, and the liver edge could not be made out. The prostate was slightly enlarged.

The temperature was 99.8°F., the pulse 85, and the respirations 20. The blood pressure was 120 systolic, 80 diastolic.

Examination of the blood revealed a hemoglobin of 13 gm. and a white-cell count of 9000. The urine was normal.

An x-ray film of the chest showed the left hilus to be low and surrounded by a homogeneous area of increased density, with irregular flamelike borders (Fig. 1). In the lateral view the density was seen to occupy the hilar area. There were increased lung markings in the region of the left lower lobe and in the base of the left upper lobe, probably representing atelectatic areas. The right lung field was clear, except for a thin linear area of increased density, which probably represented minimal atelectasis. The diaphragm was normal in position, and both costophrenic angles were clear. The heart and upper mediastinum were not remarkable.

A biopsy of the right supraclavicular node and a bronchoscopy were performed.

DIFFERENTIAL DIAGNOSIS

DR. BRIANT L. DECKER: May we see the x-ray films?

DR. JAMES R. LINGLEY: This film shows the enlargement of the left hilus that is described in the record, and in the lower portion a lobular mass can be seen. The lateral view shows the density in the region of the hilus, which I believe definitely involves the base of the upper lobe and probably of the lower lobe. The right lung is clear except for this small area of atelectasis. There is no displacement of the heart, no mediastinal enlargement, and no fluid.

DR. DECKER: Is there any collapse in the left lower lobe?

DR. LINGLEY: I think that there is probably some collapse in both lobes.

DR. DECKER: Is there any calcification?

DR. LINGLEY: No.

DR. DECKER: Is this shadow a node?

DR. LINGLEY: No; I believe that it is the transverse process of a vertebra.

DR. DECKER: This forty-seven-year-old shipping clerk had had chronic cough for two years, with only mucoid sputum, and had lost 65 pounds. He had no real chest pain but had substernal soreness and slight fever. Enlarged lymph nodes were found in the right supraclavicular region on physical examination, and there were the x-ray findings that Dr. Lingley has pointed out. I assume that the two processes — that is, the x-ray appearance and the enlarged nodes — were related. Consequently I believe that this was some type of new growth. The two most probable diagnoses are primary bronchiogenic carcinoma and lymphoma, although I lean more strongly toward carcinoma. With lymphoma of this duration one would see a mediastinal mass and would find lymph nodes in the axillas and elsewhere. I believe that when invasion of the lung occurs with lymphoma it is fairly advanced, although it may occur early on rare occasions. The weight loss could go with either condition. If it were associated with carcinoma, I should expect more extensive carcinoma than was apparent in this case. The slight temperature could also go with either. From the x-ray appearance I believe that this lesion, which caused partial obstruction of bronchi, together with metastases, was most probably an adenocarcinoma. Small-cell carcinoma usually grows much more rapidly but it does spread by the lymphatic vessels. A year, however, is too long a duration for such a tumor. Squamous-cell or epidermoid carcinoma is directly invasive and usually does not involve the lymph nodes. Adenocarcinoma travels by the blood stream, is often found in the lymphatic vessels, and frequently produces distant metastases. It is perhaps more slowly growing than

a small-cell carcinoma. I am most in favor of adenocarcinoma.

Tuberculosis, which could have produced this picture, is unlikely in a person of this age. Lymph nodes and a process of this sort could occur in a young person or in an older patient, with more extensive tuberculosis.

Sarcoid is also a possibility, although I do not believe that so much weight loss would have been noted. Sarcoid is usually bilateral and symmetrical.

The various mycoses are unlikely because the patient's occupation did not expose him to the agents that cause such diseases — he was a shipping clerk. He did not come from the Southwest, so that coccidioidal granuloma can probably be ruled out. In a chronic stage the other mycoses would have been more ulcerating, with lesions of the skin.

In conclusion I believe that this was most probably an adenocarcinoma, primary in the bronchus.

DR. TRACY B. MALLORY: Are there any other suggestions?

DR. DONALD S. KING: Dr. Sweet and I have just been talking it over, but we do not agree that adenocarcinoma is a likely diagnosis. If this was a carcinoma we believe that it was probably epidermoid.

DR. MALLORY: Dr. Miller, will you tell us what you know about the case?

DR. CARROLL MILLER: I saw this man in my office before I sent him to the hospital, and at that time he brought with him x-ray films that had been taken elsewhere. The ray formation from the central hilar mass was more marked in those plates than in the ones taken in this hospital. In both supraclavicular fossae there were nodes that were fixed, firm and rather matted together, and I believed that the diagnosis was carcinoma of the lung, with metastases to the supraclavicular fossae; although we have seen few carcinomas of the lung that metastasized in a relatively early stage to that region, such cases do occur. Because of the weight loss, the time interval and the x-ray appearance my diagnosis was carcinoma. I think that the bronchoscopic findings were interesting and similarly confusing.

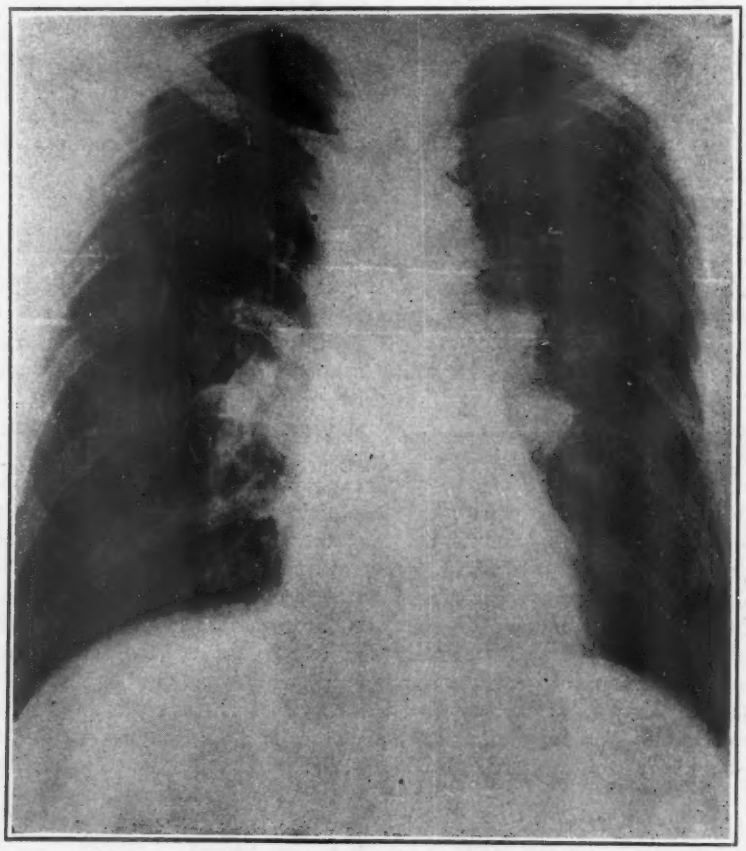

FIGURE 1. *Roentgenogram of Chest.*

CLINICAL DIAGNOSIS

Carcinoma of lung.

DR. DECKER'S DIAGNOSIS

Primary bronchiogenic adenocarcinoma.

Anatomical Diagnosis

Tuberculosis of bronchus.

Pathological Discussion

Dr. Mallory: On bronchoscopic examination a tumorlike outcropping was seen on the bronchial wall. The bronchoscopist also considered the appearance characteristic of carcinoma. The surprise came in the microscopic examination. The biopsy from the bronchus showed tuberculous granulation tissue, and that of the supraclavicular lymph node also showed frank caseous tuberculosis. The patient is now in a sanatorium.

CASE 32342

Presentation of Case

A thirty-one-year-old housewife entered the hospital because of lower abdominal pain.

The patient had apparently been in good health until six weeks before entry, when she experienced crampy lower abdominal pains associated with the menstrual period. The pains were dull and aching and radiated to both sides of the lower back. The period had begun at the usual time, but bleeding was scanty and prolonged over ten days. The periods usually occurred every twenty-eight days, lasted four or five days and required about four pads. They were never accompanied by discomfort. After this period had ended, the patient continued to suffer from intermittent attacks of similar pain. The following period came at the expected time but lasted only two days, with scanty flow. Four days before entry, about an hour after supper, the pain became markedly worse, and the patient vomited her supper. The pain continued during the night, and she vomited several more times, producing whitish "phlegm and water." Her condition remained essentially unchanged, and she continued to vomit, despite taking only fluids by mouth. Two days before entry she felt somewhat improved, vomiting only once and taking some solid food. On the day of admission, however, the pain was severer than at any previous time and she again began to vomit. At no time did the vomitus contain bile, blood or coffee-grounds material. She had had no bowel movement and little or no flatus during the four days before entry. Since the onset of the illness she had had sharp lower midline abdominal pain during urination, but passage of the urine itself caused no burning and the urine was not bloody. She had felt feverish during the illness but had had no chills. During the week before entry she had had a "slight cold," with rhinitis and some coughing.

The patient had four children aged twelve, ten, six and four years. Seven years previously she had had a miscarriage, and since the birth of her youngest child she had noticed a scant whitish discharge. Both the patient and her husband denied any venereal infection.

Physical examination revealed a well developed woman who appeared acutely ill. The heart and lungs were normal. The abdomen was distended, with diminished peristalsis and some fullness in the suprapubic region. There was diffuse and rebound tenderness, most marked in the lower abdomen, especially in the midline. Pelvic examination showed a grapefruit-sized tender mass in the left vault lying laterally and anteriorly. There was no tenderness on moving the cervix.

The temperature was 99°F., the pulse 105, and the respirations 20. The blood pressure was 120 systolic, 70 diastolic.

Examination of the blood revealed a red-cell count of 2,620,000, with 7.7 gm. of hemoglobin, and a white-cell count of 8900, with 74 per cent neutrophils. The corrected sedimentation rate was 66 mm. per hour. The chloride was 101 milliequiv. per liter, and the total protein 6.2 gm. and the nonprotein nitrogen 18 mg. per 100 cc. A blood Hinton test was negative. The urine was normal.

A plain film of the abdomen showed only a considerable amount of gas and fecal material retained in the colon, as well as gas in what appeared to be several loops of small intestine. The pelvis was filled by a homogeneous mass of increased density that was consistent with a full bladder.

Cultures of the cervix were negative for gonococci.

On the evening of the first hospital day the temperature rose to 99.8°F., and the patient was placed on sulfadiazine and penicillin. On this regime the mass felt by vaginal examination seemed to be decreasing in size and was definitely confined to the broad ligament. The subjective symptoms also subsided until the sixteenth hospital day, when the pain in both lower quadrants returned. On the twenty-first hospital day a peritoneoscopy revealed a questionable cyst of the right ovary. On the twenty-sixth hospital day an operation was performed.

Differential Diagnosis

Dr. John B. McKittrick: This thirty-one-year-old mother of four children, previously in excellent health, entered the hospital with the complaint of lower abdominal pains of six weeks' duration. The pains which were first noted in association with a menstrual period, were dull and aching and radiated to both sides of the lower back. The period had started in a perfectly normal fashion except that bleeding was scanty and prolonged for ten days; this was distinctly unusual, since the patient had never had discomfort with her periods and the menses had usually lasted four or five days. The amount of flow was abnormal, as were the duration and, of course, the pain. When the actual menstrual flow had ceased, the pain continued in an intermittent fashion but apparently did not change in

character. The next period came at the proper interval but was abnormal in that it lasted only two days and the flow was again scanty. This second menstrual period apparently occurred about two weeks before admission to the hospital. Four days before admission, shortly after supper, the pain became much severer and more protracted and was accompanied by repeated vomiting throughout the night of food recently eaten. Two days later the patient improved somewhat. The vomiting was less persistent, and she was able to take a small amount of solid food. On the day of admission, however, there was a sharp recrudescence of the pain and vomiting also returned; at all times the vomitus was free of blood and bile. During this four-day period, during which the symptoms had altered and become severer, a new element was introduced, namely, absence of bowel movements associated with the passage of little or no flatus. Another symptomatic clue is that during the course of the illness the patient had sharp discomfort on urination, but the passage of urine was not associated with burning and the urine was apparently normal. The patient stated that she had had no chills during the course of her illness but at times had felt feverish.

It seems clear that some acute process was going on and was localized to the abdomen and associated with the genital system. What could have caused such an abrupt change in the menstrual cycle, associated with low abdominal pain radiating through to the back and with involvement of the intestinal tract in a way that interfered with intestinal motility? Several things come to mind. Was this an inflammatory process? The patient felt feverish but had no chills. Beyond that there is no indication of how prostrated she had been by the illness. It is perfectly conceivable that pelvic inflammatory disease could persist for six weeks, becoming acute, involving the intestinal tract, — usually the small bowel, — and causing intestinal obstruction. As a rule, however, such patients are rather acutely ill, with a high fever; they frequently have chills, and when the process is as acute as this seemed to be, there is usually associated urinary symptomatology. Acute appendicitis, which frequently causes this type of abdominal pain and low-grade fever, must be considered. A patient may present such a history of several weeks' duration and may consult a physician only when symptoms become much severer as in the case under discussion. Was this a benign tumor, such as an ovarian cyst, that during a period of six weeks was intermittently and finally irreducibly twisted and caused the acute symptomatology for the last four days before admission? Such a tumor is rather unlikely, although most of the symptoms could be explained on that basis. As a rule, ovarian cysts do not cause the disturbance in the menstrual cycle that occurred in this case. They cause nausea and vomiting, as well as the type of pain that the patient complained of, but not usually the degree of disturbance in intestinal motility that was apparently present. I think that one need mention malignant tumor only to be complete, but there was no evidence that this process was anything but acute. By a process of rapid elimination one arrives at the diagnosis that seems to fit this whole problem best — namely, some type of extrauterine pregnancy which could account for the change in the menstrual history, as well as the pain and the intestinal symptoms.

On admission to the hospital the patient was well developed and acutely ill. Physical findings were limited to the abdomen, which was distended. There were diminished peristalsis and suprapubic fullness. Diffuse tenderness and rebound tenderness were most marked in the lower abdomen, near the midline. Pelvic examination showed a grapefruit-sized tender mass lying to the left and anteriorly. There was no tenderness on moving the cervix. The temperature was 99°F., the pulse 105, and the respirations 20. The blood pressure, I am interested to note, was normal. Examination of the blood showed a red-cell count of 2,600,000, with a hemoglobin of 7.7 gm., and a normal white-cell count, with 74 per cent neutrophils; the corrected sedimentation rate was 66 mm. per hour. Other studies, including the chloride, protein and nonprotein nitrogen levels and the blood Hinton reaction, were negative. Examination of the urine was also negative. A plain film of the abdomen confirmed the clinical impression of an excessive amount of retained gas and fecal material in both the large and the small bowel — primarily the former — and in addition revealed the mass palpated by the examiner, which was interpreted as being consistent with a full bladder. Apparently there were no characteristic features about this mass, but that is not surprising. Cultures of the cervix were negative for gonococci. The record does not give a vital bit of information that I am sure was determined: the results of the test for pregnancy. I do not see how one could examine this patient and listen to her history without considering that question.

In summary, this patient was acutely ill, with a mass in the pelvis, an altered menstrual cycle, and evidence of intestinal dysfunction but little suggestion of an acute inflammatory process — certainly not an inflammatory process that was causing much of a systemic reaction. The temperature was only slightly elevated, and the white-cell count was normal, although there was an elevated sedimentation rate, the upper limit of normal in this hospital being 20 mm. Just what does that mean? It is perfectly true that in some cases the sedimentation rate is elevated out of proportion to other evidences of inflammation, such as the temperature and the white-cell count, in the presence of venereal infection in the pelvic organs, and it is entirely possible that this patient had such an infection despite the negative culture and the absence of other symptoms

usually associated with acute pelvic inflammatory disease. The sedimentation rate, however, cannot be depended on to differentiate pelvic inflammatory disease and acute appendicitis. I have mentioned acute appendicitis, and I cannot completely exclude it as the cause of the trouble. The degree of ileus (I say "ileus" rather than obstruction because the distribution of the gas shadows was mostly in the large bowel, and at any rate there was certainly no small-bowel obstruction) is entirely consistent with an appendiceal abscess, as were the pain and vomiting The unusual position of the mass — on the left and anteriorly — and the change in menstrual rhythm are strong evidence against appendiceal abscess. The presence of pelvic inflammatory disease might also account for what I believe to have been an extrauterine pregnancy. Pathologic changes that occur in the tubes following inflammatory disease predispose a patient to such difficulties. On the basis of the way the patient was handled in the hospital, I assume that the condition was considered to be acute pelvic inflammatory disease with probably a tubo-ovarian abscess, since she was treated conservatively until the twenty-sixth hospital day, when she was operated on; the negative culture from the cervix does not exclude pelvic inflammatory disease. If the diagnosis had been extrauterine pregnancy, operation would probably have been performed somewhat earlier. Despite the delay in operation, however, I believe that extrauterine pregnancy offers the best explanation for the anemia, the mass, the ileus, the absence of symptoms referable purely to infection and the change in menstrual cycle. I also believe that the pregnancy was not tubal but abdominal, possibly either ovarian or located in the broad ligament itself. I exclude tubal pregnancy because it does not, as a rule, persist for such a long time without causing dramatic symptoms when there is rupture and enough bleeding to lower the hemoglobin to 7.7 gm. Apparently the process in this patient had bled, but the bleeding was not sufficiently acute or severe to produce shock, which is almost certain to follow when the tubal pregnancy reaches the stage of rupture into the preperitoneal cavity. She may have had an element of inflammatory disease, which I think was secondary.

My diagnosis, therefore. is extrauterine pregnancy, probably abdominal, with or without low-grade pelvic inflammatory disease.

Clinical Diagnoses

Ovarian cyst.
Pelvic inflammatory disease?

Dr. McKittrick's Diagnosis

Extrauterine pregnancy, probably abdominal.

Anatomical Diagnosis

Abdominal pregnancy.

Pathological Discussion

Dr. Tracy B. Mallory: There was only one omission, an unintentional one, from this patient's history. She had had her appendix removed at the age of eighteen. If Dr. McKittrick had known this, one confusing factor would have been eliminated. No Aschheim–Zondek test was ever done, and if the diagnosis of pregnancy was seriously considered, such an impression was not recorded. Opinion first favored pelvic inflammatory disease and then shifted to ovarian cyst. The patient was eventually explored, with the latter as the preoperative diagnosis.

At operation a moderate amount of free blood was encountered when the peritoneal cavity was opened. A large mass was found in the left side of the pelvis posterior to the broad ligament and covered by adherent omentum. When the omental adhesions were freed a cavity was broken into, out of which a fetus measuring 9 cm. in length was extruded. A well developed placenta was adherent to the fimbria of the left fallopian tube. There was considerable old clotted blood in the posterior cul-de-sac. A left salpingectomy was done as the simplest method of dealing with the placental implantation. The pregnancy, however, was definitely extratubal and intra-abdominal, as Dr. McKittrick predicted.

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GRADUATES OF NONAPPROVED MEDICAL SCHOOLS

A letter published elsewhere in this issue of the *Journal* calls attention again to the difficulties that graduates of nonapproved schools who served as medical officers during the war are having in obtaining additional medical training, particularly as residents in the hospitals of the Veterans Administration. Any unprejudiced discussion of the problem should be based on facts rather than on assumptions, and it seems necessary to question some of the statements contained in the letter.

In the first place, although the majority of graduates of nonapproved schools may have "really felt the 'call' to medicine," most of them were undoubtedly refused admission to approved schools because of a premedical training that was judged to be relatively inadequate. This, combined with a medical education that failed to provide facilities comparable with those available in approved schools, places a severe handicap on such graduates, which is the obvious reason why so many of them fail to pass board examinations in the states whose statutes permit them to apply for licensure.

Secondly, state medical examining boards are not "closely regulated and governed by the American Medical Association": each state has its own medical practice act. Nor are the specialty boards "by-products" of the American Medical Association. The American Board of Surgery, for example, arose following initial efforts by the American Surgical Association, being finally created by the Advisory Board of Medical Specialties after the field had been approved by the Council on Medical Education and Hospitals of the American Medical Association. This board has thirteen members, only three of whom represent the American Medical Association.

Thirdly, it should be emphasized that practically all graduates of nonapproved schools who recently served as medical officers came from two states, — Illinois and Massachusetts, — since these are the only states that regularly permit such graduates to apply for licensure.

When all is said and done, the problems of the graduates of nonapproved schools practically limit themselves to Illinois and Massachusetts, and at least in the latter, efforts are being made to provide these men with further opportunities. All such graduates are eligible to apply for membership in the Massachusetts Medical Society five years after they have been licensed to practice. The Gallupe Plan, commented on editorially in the April 25 issue of the *Journal*, offers to these men hospital affiliation; it is sponsored by the Massachusetts Medical Society and the Massachusetts Hospital Association and has the approval of the Council on Medical Education and Hospitals of the American Medical Association and of the American College of Surgeons. Finally, during the past year the Massachusetts Medical Society has conducted courses of postgraduate medical instruction throughout the Commonwealth that have been open to all physicians. It is true that in Massachusetts there is a distinction between the

graduates of approved and nonapproved schools; on the other hand, the proper authorities appear to be doing all that they can to help the latter in improving their medical training.

In any discussion concerning the appointment of graduates of nonapproved medical schools as residents in hospitals of the Veterans Administration, it is essential to differentiate two types of institutions — "hospitals" and "affiliated hospitals." The former are solely under the control of the Veterans Administration, and graduates of nonapproved schools have been accepted as residents in these hospitals. The latter, on the other hand, are run in connection with various medical schools and are in the process of being converted into teaching hospitals for those who are desirous of qualifying for certification by one of the specialty boards. The selection of residents is subject to the approval of a committee representing the affiliated medical school or schools, — the Dean's Committee in Massachusetts, — and an attempt is made to select only those men who seem likeliest to pass the examinations of their respective specialty boards on the termination of their training. Many graduates of approved schools in the United States and Canada have been turned down, but at least in Massachusetts, some men who do not so qualify have been accepted. Although existing regulations bar the latter from certification by the majority of specialty boards, there is no doubt that the Dean's Committee will do its utmost to make their certification possible, provided that they creditably complete their residencies.

Although the path of the graduates of nonapproved schools is not easy, it appears that those who have shown industry, professional skill and a desire to better themselves have more opportunities now than ever before.

SELF-DEMAND IN INFANT FEEDING

An ancient fact has been rediscovered as a new theory in infant feeding and, being put to the test, has again been proved, namely, that babies who are fed when they are hungry are in the main happier than babies who are put to nurse when they are not hungry and are denied nourishment when they ask for it. We are witnessing now, in these matters, a pleasant swing from a gravely pontifical attitude toward the training of the very young to a rather indulgent point of view, admitting that babies are human beings like, for instance, ourselves.

We may be sure that this so-called "self-demand regime" is a relative innovation only among the more cultured classes and that many babies less fortunately situated in other ways have had certain vital needs attended to more promptly, even if in a less determinedly organized fashion. This particular swing away from the regimentation of infancy that accompanied the birth of the specialty pediatrics was initiated, or at least blessed, by that ardent student of infant behavior, Arnold Gesell.

As early as 1937, Gesell and Ilg[1] expressed themselves on this point as follows:

> Superficially it might appear that the self-demand schedule would encourage whims and instability in the child. Exactly the opposite is true. For by individualization of feeding the infant is most directly and most completely satisfied. He is satisfied vegetatively and emotionally. He escapes periods of want, anxiety and distress. The promptness and the certainty of satisfaction cumulatively experienced * * * will nourish that sense of security which is essential to mental health.

Other experimenters in this naturalistic method of feeding babies when they are hungry and not forcing them to eat at other times are presenting the results of their own explorations. Notable among these, Trainham, Pilafian and Kraft,[2] one of the authors being the mother, allowed a pair of lusty, breast-fed twins to write their own tickets for thirteen long months. The results were eminently satisfactory to the infants, although the mother, at times, found herself producing and serving as many as ten meals in a day. This, however, was an unusual case.

On the whole we must accept the obvious conclusion that the inflexibility of a mathematical attitude has been allowed to prevail much too far in the care of an extremely unmathematical subject. We have fallen into the error of believing that fixed quantities of food of prescribed caloric value must be absorbed by infants of certain weights and ages at regular intervals and in a stated number of minutes. Far better is it that more babies, at least during the early weeks of their infancy, should be allowed to benefit from the examples set by these articulate observers and the host of more humble infant guardians who always fed by the baby rather

than by the clock. After a few days or a few weeks, in most cases, the baby can be led — not forced — to accept a schedule more in accordance with that which his parents would like to follow.

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MASSACHUSETTS MEDICAL SOCIETY

DEATHS

HUBER — Edward G. Huber, M.D., of Waban, died July 23. He was in his sixty-fifth year.

Dr. Huber was born in Menomonie, Wisconsin, graduated from the University of Michigan in 1903 and received his medical degree from its medical school in 1905. After a short period of private practice in Missouri, he entered the Army Medical School, graduating in 1908. Following service in the Philippines, he was sent to France during World War I and was in command of a hospital center. While assigned to the First Corps Area, he attended and graduated from the Harvard School of Public Health in 1923. He retired from the Army in 1935 with the rank of colonel, and then accepted a position in the Massachusetts Department of Public Health, as well as an instructorship in the Harvard School of Public Health. He was appointed acting dean of the latter in 1942 and was made associate dean and professor of public health at the time of the recent organization of the school, in which he took an extremely active part. He was a member of the American College of Physicians and a fellow of the American Medical Association.

His widow and a daughter survive.

KINNEY — William D. Kinney, M D., of Osterville, died July 12. He was in his seventy-fourth year.

Dr. Kinney received his degree from Bowdoin Medical School in 1899 and had practiced in Osterville for nearly half a century. He had been associate medical examiner of Barnstable County for twenty years and had always been active in the affairs of the Massachusetts Medical Society, having been a member of the Council and a supervising censor for many years, as well as president of his district society from 1913 to 1915.

His widow and a son survive.

STACEY — Charles F. Stacey, M.D., of Blue Hill, Maine (formerly of Boston), died July 18. He was in his eightieth year.

Dr. Stacey received his degree from Harvard Medical School in 1892. He was a member of the Massachusetts Medical Society and a fellow of the American Medical Association.

His widow survives.

NEW HAMPSHIRE MEDICAL SOCIETY

DEATH

CLAGGETT — Fred P. Claggett, M.D., of Newport, died July 4. He was in his seventy-eighth year.

Dr. Claggett received his degree from Dartmouth Medical School in 1897. He was a former president of the Sullivan County Medical Society and a fellow of the American Medical Association.

A son and two daughters survive.

MEDICOLEGAL ABSTRACT

Relation of Patient and Physician: Liability for malpractice. A recent decision of the Supreme Judicial Court of Massachusetts contains several points of interest to the medical profession. The action concerned a claim for so negligently treating a throat ailment as to cause the plaintiff's intestate to die.

On November 24, 1941, the intestate was suffering from a severe cold. Two days later he complained of a sore throat. He did not respond to tablets and a gargle prescribed by a physician other than the defendant. On November 27 he was admitted to a hospital conducted by the defendant. On November 28 the patient's wife, who had worked as a practical nurse for ten years, saw him; he was very ill and cold, complained of pain in his sides, and was coughing. On November 29, when his wife again saw him, his face was flushed and he was coughing up brownish sputum. She told the floor nurse that he had pneumonia. In stating the case the court said:

> If a person has a cough, a previous history of a cold and a pain in his sides, and complains of being cold, the defendant would be suspicious that pneumonia had started; and if on the next day he discovered a definite dullness on percussion of the chest, an increase in the voice sounds, bronchial or harsh breathing sounds, a flushing of the face, a high temperature and the common symptom of a rusty colored sputum containing dark-brown blood, a definite diagnosis of pneumonia could then be made. A hospital record, in the handwriting of the defendant, stated that the lungs of the intestate were clear on November 27, 1941, and on November 30, 1941. According to this record, the intestate on November 30, 1941, was objecting rather violently to treatment and to taking nourishment. The defendant called upon the welfare authorities to remove the intestate from the hospital. On the afternoon of November 30, 1941, he was driven in an automobile by a police officer sixty to seventy miles to the Tewksbury State Hospital. An examination at this hospital on the morning of December 1, 1941, disclosed that there was "bronchovesicular breathing at the left base with coarse rales throughout." The examining physician suspected that the intestate had pneumonia. The intestate died on the evening of December 1, 1941.
>
> It was undisputed that the intestate was suffering from Vincent's angina when he was admitted to the defendant's hospital. This disease starts with a laceration of the pharynx in the region of the tonsils, and as it progresses involves the entire mucous coating of the mouth. The temperature and pulse are increased and the patient becomes very ill. There may be chills and the sputum becomes rusty colored . . . .

The defendant apparently admitted that it would be improper practice for an X——— doctor to remove a patient from X——— to Tewksbury knowing that he had pneumonia, since such removal might use up his strength and cause his death. An expert testified that if a patient had Vincent's angina and if it was known that he also had pneumonia, it was bad medical practice for the defendant to order his removal from X——— to Tewksbury. The court was of the opinion that the question was proper, because there was evidence that the defendant should have known that the intestate had

pneumonia. Where this evidence came from is not clear from the opinion.

After the expert testified as above, further examination revealed that he was not familiar with X——— practice. Subsequently he was asked whether it was proper practice for a physician *in a town the size of X———* to permit a man with a temperature of 100°F. to be moved some sixty miles. Although the layman might suppose that any well qualified doctor could answer such a question, it has long been an established rule of law that the standard of care required of a doctor depends on the standards of the particular community in which he practices, and since the witness admitted lack of knowledge concerning X——— practice, the trial judge could not properly allow him to answer this question when it was objected to by the defense.

The jury found for the plaintiff, and the court was of the opinion that the evidence was sufficient to warrant such a finding.

The plaintiff's declaration was for death caused by the negligent treatment of a sore throat. The evidence was such that the jury could believe that death was caused by the improper removal of the intestate from X——— to Tewksbury. Ordinarily a physician may discontinue treatment of a patient without incurring liability, if his treatment, up to the time of discontinuance, has been proper. In this case the physician was liable because the manner in which he discontinued the treatment was in itself the cause of injury to the patient. — 1946 Adv. Sh. 945, July 8, 1946.

CORRESPONDENCE

CHIGGERS IN MASSACHUSETTS

To the Editor: This brief report I believe is justified, since it has generally been assumed that New England is free from chigger, the six-legged larva of the mite *Trombicula alfreddugesi*, otherwise known as harvest mite or red bug.

I recently saw a family of four who had a ways lived in the heart of New York City but who had lately bought an abandoned estate in Plymouth. They all had bad cases of poison ivy, but they also presented a rash, especially on the legs, which to my mind was typical of chigger infestation, since I had had a chance one summer to see a large number of cases in North Carolina and Tennessee. As it was night, it was impossible to look for the causative insect, but the following morning the family captured some and sent them to me, preserved in toilet water. There was no question whatever about their identity, but to be absolutely sure, I sent them to Dr. Howard J. Parkhurst, of Toledo, Ohio, who is unquestionably this country's expert on chigger. He kindly identified them for me.

There also appears to be a focus of infestation in Hyannis, although I have so far been unable to capture any of the insects.

Chigger infestation is of common occurrence throughout the South and up through the central states to the Great Lakes, but it has been supposed to stop in its northeastward distribution somewhere in Pennsylvania and New Jersey.

AUSTIN W. CHEEVER, M.D.

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GRADUATES OF NONAPPROVED MEDICAL SCHOOLS

To the Editor: In concurring with Dr. John D. Lane's letter in the June 13 issue of the *Journal*, I should like to take this opportunity to elaborate further on the subject of discrimination against medical graduates of unapproved schools.

The majority of these men who have knowingly attended unapproved schools did so because they really felt the "call" to medicine. There was no family desire for a doctor nor the glory of being called a "doctor." The love for the profession of their calling and their desire to help their fellow man drove them on to acquire the necessary knowledge. This drive had to be very strong in order to overcome the obstacles thrown in their path by the American Medical Association's rules and regulations. As a result they received more out of their education in medicine because they had to put more into it to compete with graduates of approved schools.

Many graduates of unapproved schools entered the various branches of the armed forces during the past emergency as medical officers, and in every way competed on equal footing with other medical officers. They were equally exposed to the same dangers, hardships, injuries and death as medical officers of approved schools and in many instances were decorated for bravery for extraordinary performance of duty. Therefore, it came as a great surprise to the writer that on inquiring from the Department of Medicine and Surgery of the Veterans Administration he was informed that even though graduates of unapproved medical schools are considered veterans, and were considered to have the necessary education and ability to treat the boys during the war and on the battlefields, now they are not considered capable of being assigned as residents in the veterans' hospitals. In other words, the American Medical Association and its by-products, namely the specialty boards, will not permit graduates of unapproved schools who served as medical officers in one of the branches of the armed forces to be appointed as residents. They have by this means prevented these men from further learning and training, which would allow them to treat their fellow man with the best possible knowledge and methods available.

I have repeatedly sent letters to the Department of Medicine and Surgery of the Veterans Administration on this point, and they pass the buck on to the specialty boards — in my case the American Board of Surgery. In corresponding with the secretary of this board my question "whether or not a veterans' hospital would lose its residency status if it appointed veterans of World War II who are graduates of an unapproved school as residents" is repeatedly and completely ignored. Therefore, it appears to me that if the Veterans Administration is passing the buck, and in so doing preventing graduates of unapproved schools from keeping up with new methods and treatments in their field of endeavor, it is showing once again the obstacles put before these men by the mighty powers of the American Medical Association.

It should also be called to the attention of those in power that the restrictions of hospital privileges and the right to practice their profession in whatever state they so desire are a definite form of discrimination. These privileges should be allowed to all graduates of legally chartered medical schools who have passed the examinations given to graduates of approved schools and who have served an approved internship. The refusal of allowing these privileges is fully as undemocratic as under a dictatorship. The rules of the various state medical examining boards are closely regulated and governed by the American Medical Association.

I should like to close with the final statement, which I believe hits the nail on the head: "A school never made a man — a man makes a school."

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BOOK REVIEWS

Your Hair and Its Care. By Oscar L. Levin, M.D., and Howard T. Behrman, M.D. 12°, cloth, 184 pp. New York: Emerson Books, Incorporated, 1945. $2.00.

This book, written for the lay reader, does not contain too much scientific material. The style is clear and concise, and the advice contained is quite sensible. It is a book that can be read with profit and enjoyment by both physician and patient. The final chapter, entitled "Questions and Answers," gives an excellent condensed summary of recent scientific knowledge concerning the anatomy, physiology, pathology and proper care of the scalp.

Bone-Grafting in the Treatment of Fractures. By J. R. Armstrong, M.D., M.Ch., F.R.C.S. With a foreword by R. Watson-Jones, B.Sc., M.Ch.Orth., F.R.C.S. 8°, cloth, 175 pp., with 204 illustrations. Baltimore: Williams and Wilkins Company, 1945. $7.00.

This well written and effectively illustrated book should find a ready welcome among those who treat a large number of fractures. Methods of bone grafting are described for fractures of the spine and of the upper and lower extremity; the author usually prefers an onlay graft obtained from the tibia, which is fixed in place with nonoxidizing metal screws. Prolonged immobilization in plaster accompanied and followed by reconditioning exercises is advocated. For these procedures the no-touch technic is practiced. For the most part the author follows the usual indications for operative treatment of fractures, but in his enthusiasm he advocates its use much earlier in many cases than would be considered wise in American clinics.

A foreword by Sir Reginald Watson-Jones gives a timely warning concerning infection. Although bone grafting as the author describes it is a most valuable aid in the treatment of a number of difficult fractures, it is a matter not to be undertaken lightly, for infection is worse than nonunion or malalignment.

Penicillin and Other Antibiotic Agents. By Wallace E. Herrell, M.D., M.S. 8°, cloth, 348 pp., with 45 illustrations and 45 tables. Philadelphia: W. B. Saunders Company, 1945. $5.00.

Publications of the Mayo Clinic bear unmistakable hallmarks: almost invariably they are well printed and clearly illustrated, are written in simple, understandable style, include a good bibliography, and are accurately and comprehensively indexed. This volume is typical of such publications.

The subject matter is divided into four parts of approximately the same length. The first part gives an admirable account of the development of penicillin, describes its method of preparation, its physical and chemical properties, how it behaves in contact with bacteria, how it is standardized, and how its concentration in body fluids can best be measured. The second and third parts are clinical. The reader unfamiliar with penicillin will find these pages of particular interest. The conditions in which the use of penicillin is indicated are well described, as is its proper method of administration and dosage. The illustrations help to make the text more interesting and more easily understood. The fourth part discusses other antibiotic agents — tyrothricin, streptothricin, streptomycin and similar substances — and brings out the far-reaching developments in medical research that the work of Dubos with gramicidin and of Fleming with penicillin has already stimulated.

Not many years ago the science of pharmacology appeared to be sluggish; chemotherapy and the discovery of antibiotics have opened an entirely new chapter in medical history, which is being studied with astonishing diligence. This book tells the whole story in an engaging fashion. It is a readable, informative and useful contribution.

NOTICES

ANNOUNCEMENT

Dr. Virgil G. Casten, having returned from over five years of naval service, has resumed the practice of ophthalmology at 412 Beacon Street, Boston.

AMERICAN DIABETES ASSOCIATION

The American Diabetes Association will hold its sixth annual session on September 16 to 18, 1946 in Toronto, Canada. The first day of the meeting will be devoted to celebrating the twenty-fifth anniversary of the discovery of insulin. The program has been arranged by the University of Toronto and will feature distinguished guests from government and medical circles. Among the latter will be Drs. C. H. Best and W. R. Campbell from Canada, Drs. E. P. Joslin, R. M. Wilder, Seale Harris, David P. Barr, and Eugene Opie from the United States, Dr. R. D. Lawrence from England, Dr. H. C. Hagedorn from Denmark and Dr. B. A. Houssay from Argentina. On the second day, the program has as its theme a review of the accomplishments of the past twenty-five years in various aspects of diabetes. Papers will be presented on diet, insulin, coma, gangrene, pregnancy and longevity. The third day will be divided into two sessions. The morning will consist of a presentation of experimental work and research in various phases of insulin and diabetes. The afternoon session will feature a series of short papers on recent investigations in the complications of diabetes. This will be followed by an open forum presided over by Dr. R. M. Wilder, incoming president of the American Diabetes Association. There will be a board of experts who will answer questions from the floor, in a "Stump the Experts" quiz program.

This elaborate program promises to be a fitting tribute to the memory of Dr. Frederick Banting.

CONGRESS ON INDUSTRIAL HEALTH

The schedule of events for the seventh annual Congress on Industrial Health, which is to be held at the Copley-Plaza Hotel, Boston, September 30 through October 2, is as follows:

Monday, September 30:

Clinical Toxicological Conference	
Topic — "Lead Poisoning"	All day
Surgical Conference	
Topic — "The Foot in Industry"	Afternoon
Professional Relations Conference and Dinner	Evening

Tuesday, October 1:

General Session	Morning
Topic — "Human Relations in Industry"	
Elective Seminars	Afternoon
Section A — Industrial Physiology	
Section B — Administrative Methods	
Section C — Workmen's Compensation	
Dinner and Conference on Pan-American Industrial Health	Evening

Wednesday, October 2:

General Session	Morning
Topic — "Atomic Energy: Its effects in industry and medicine"	Afternoon
General Session	Afternoon
Topic — "A Positive Health Program for Industry"	
Dinner and Conference on Health and Welfare Programs in Industry	Evening

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NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, September 5, in the classroom of the Nurses' Residence at 7:15 p.m. Dr. Felicia A. Banas will discuss mesenteric thrombosis, and Dr. Wyland F. Leadbetter, genitourinary tuberculosis. Dr. Grace E. Rochford will be chairman.

(*Notices continued on page xvii*)

NOTICES (*Continued from page 284*)

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Thursday, August 29

Tuesday, September 3
*12:15–1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.

Wednesday, September 4
*10:30–11:30 a.m. Medical Clinic. Isolation Building Amphitheater. Children's Hospital.
*12:00 m. Clinicopathological Conference. (Children's Hospital.) Amphitheater, Peter Bent Brigham Hospital.
*2:30–4:00 p.m. Combined Clinic by the Medical, Surgical and Orthopedic Services. Amphitheater, Children's Hospital.

*Open to the medical profession.

March 15–September 15. Boston University Course for Discharged Medical Officers. Page 240, issue of February 14.
September 4–7. American Congress of Physical Medicine. Page 616, issue of May 2.
September 5. New England Hospital for Women and Children. Page 284.
September 12. Bronchiectasis and Pulmonary Abscess: Diagnosis and treatment. Dr. Maurice Segal. Pentucket Association of Physicians. 8:30 p.m. Haverhill.
September 16–18. American Diabetes Association. Page 284.
September 30–October 2. Congress on Industrial Health. Page 284.
October 6–12. Interamerican Congress of Cardiology. Page xix, issue of June 6.
October 7–12. Seminar in Legal Medicine. Page 206, issue of August 8.
October 7–18. New York Academy of Medicine. Page 544, issue of April 18.
February 7. American Board of Obstetrics and Gynecology. Page 238, issue of August 15.
April 28–May 2. American College of Physicians. Page 206, issue of August 8.

District Medical Society

PLYMOUTH

October. Jordan Hospital, Plymouth.
November. Plymouth County Hospital, South Hanson.
January. Brockton Hospital, Brockton.
February. Moore Hospital, Brockton.
March. Goddard Hospital, Brockton.
April. State Farm, Bridgewater.
May. Lakeville Sanatorium, Lakeville.

BOSTON CITY HOSPITAL

Postgraduate Courses

Refresher Course in Medicine. This is a sixteen-week course conducted by the Boston University, Harvard and Tufts medical services of Boston City Hospital. The course is designed to emphasize practical instruction. It will consist of a clinical clerkship on the medical wards (eight weeks) and special medical clinics in the Out-Patient Department (eight weeks), under supervision of instructors from all three teaching units. In addition, daily formal exercises including clinics, conferences and lectures will be held which all students will attend. Enrollment for this course will be limited to twenty-four students (eight to each teaching unit) for each sixteen-week period. No special books will be required for this course. **Fee $230.00.**

Refresher Course in Pathology. This course will comprise a twenty-four-week review of autopsy and surgical material at the Mallory Institute of Pathology under the supervision of Drs. F. Parker, Jr., G. K. Mallory and S. L. Robbins. The systematized review of pathologic anatomy will include lectures, conferences and participation in autopsies and the examination of surgical specimens. The course is designed to give a thorough postgraduate training in pathology, with a view to satisfying the needs of the various American specialty boards. It is limited to eight members for each twenty-four-week period. **Fee $350.00.**

These courses begin on October 1, 1946, and are open to all properly qualified physicians. They have been approved by the Committee for Hospital Training Programs under Public Law No. 346 (Further Training of Veterans).

Requests for application blanks or further information should be addressed to Dr. John P. Rattigan, Co-ordinator of Interns, Boston City Hospital, 818 Harrison Avenue, Boston 18.

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